

ULF BERG

**A STUDY OF CARBOCYCLIC AND HETEROCYCLIC QUINONE METHIDES,
AND OF SOME AROMATIC THIOAMIDES.**

BARRIERS TO INTERNAL ROTATION AND PPP CALCULATIONS

Lund 1974

A STUDY OF CARBOCYCLIC AND HETEROCYCLIC QUINONE METHIDES,
AND OF SOME AROMATIC THIOAMIDES.

Barriers to internal rotation and PPP calculations.

Ulf Berg, fil. kand., Ld.





ACKNOWLEDGEMENTS

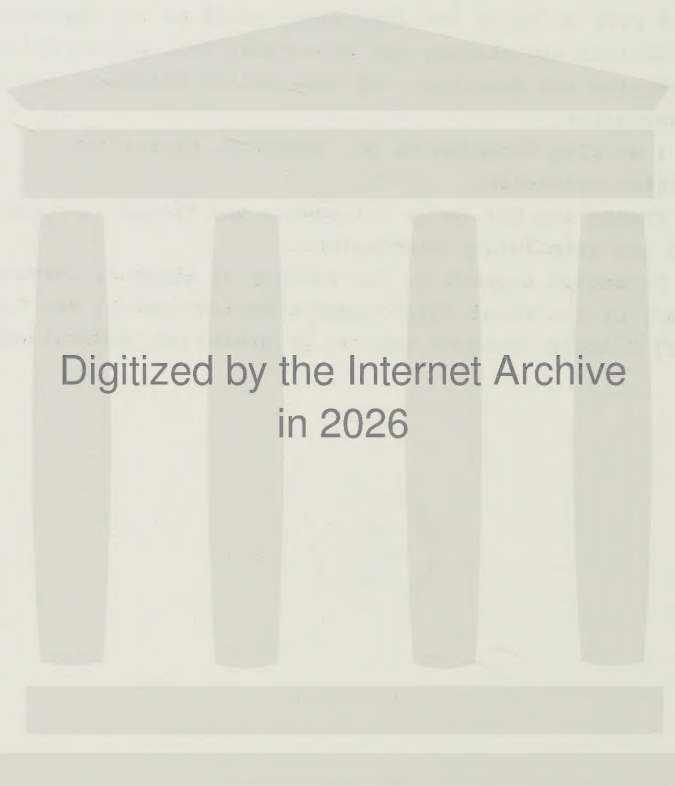
I would like to express my deep gratitude to Professor Jan Sandström for his encouraging and helpful guidance of the work presented in this thesis.

I wish to thank the laboratory staff of the department for technical assistance, and especially Mrs. Britta Maltesson, who prepared the drawings, and Miss Heleen Molenaar, who typed the manuscript.

I am also indebted to Dr. Robert E. Carter for linguistic criticism.

Thanks are due to my colleagues and friends for good advice and stimulating discussions.

Financial support by the Faculty of Science, University of Lund, by the Royal Physiographic Society and by the Swedish Natural Science Research Council is gratefully acknowledged.



Digitized by the Internet Archive
in 2026

CONTENTS

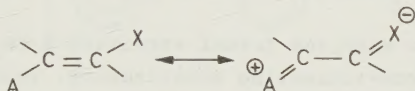
I.	SURVEY	7
II.	SYNTHETIC METHODS	8
II.1	Hydroxyaryl-dithioesters	9
II.2	N,N-Dimethyl-hydroxyaryl-thioamides	12
II.3	Quinone methides	17
II.4	Azolinones	19
III.	METHODS FOR THE EVALUATION OF RATE CONSTANTS FROM NMR SPECTRA	26
IV.	HYDROXY AND METHOXY SUBSTITUTED AROMATIC THIOAMIDES	32
IV.1	Introduction	32
IV.2	Results of barrier measurements	34
IV.3	Infrared and NMR data on hydrogen bonding	40
IV.4	Discussion of the barriers	47
IV.5	Entropy of activation	54
IV.6	Ultraviolet spectra	55
V.	QUINONE METHIDES	64
V.1	Introduction	64
V.2	Results and discussion of the spectra of the individual compounds	67
V.3	Conclusions	78
VI.	AZOLINONES	82
VI.1	Introduction	82
VI.2	Results of barrier measurements	82
VI.3	Concentration dependence of the rotational barriers	84
VI.4	Catalytic effects of acid and base and of impurities	84

VI.5	Discussion of the barriers	89
VI.6	Effects of acid and solvent	93
VI.7	Molecular orbital calculations	95
VI.8	Geometries	98
VI.9	Calculation of rotational barriers	101
VI.10	Results of the calculations	101
VI.11	Ultraviolet spectra	104
VII.	EXPERIMENTAL	111
	REFERENCES	128

I. SURVEY

The work described in this thesis concerns the subject of barriers to internal rotation in polarized, conjugated systems, as studied by NMR measurements.

The interaction between an electron-donating group (A) and an electron-withdrawing group (X) across a conjugated system is qualitatively described by the two resonance structures:



The degree to which the polarized structure contributes to the resonance hybrid is determined by the properties of the groups A and X, and it is felt that this interaction will be reflected in the rotational barriers around the A-C, C=C and C-X bonds. This has also been confirmed for several classes of compounds, as reviewed by Binsch,¹ Sutherland² and Kalinowski and Kessler.³

This study is divided into three parts, two of which concern rotation around carbon-carbon double bonds in push-pull substituted ethylenes with methylthio and dimethylamino groups as electron-donating substituents and a cyclic system, which by taking up one electron pair may assume aromatic character, as electron accepting group. Both carbocyclic rings (quinone methides, Chapter V) and heterocyclic rings (azolinones, Chapter VI) have been studied. The experimental observations (rotational barriers and ultraviolet spectra) have been compared with results obtained from molecular orbital calculations.

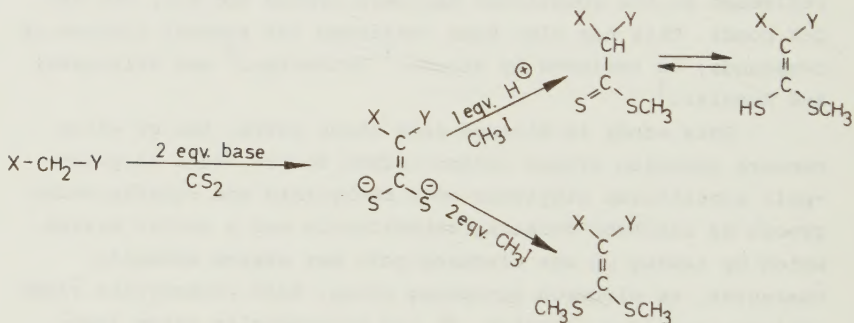
The third part treats hindered internal rotation of the dimethylamino group in N,N-dimethylthiobenzamides and thionaphthamides substituted with hydroxy groups and methoxy groups in the ortho and para positions (Chapter IV). Special attention has been given to the effect of hydrogen bonding on

the barrier heights. The existence and strength of intramolecular and intermolecular hydrogen bonds have been demonstrated by IR, NMR and UV methods.

The syntheses of the compounds studied in this work are described in Chapter II, and the methods for the evaluation of rate constants from NMR spectra are presented in Chapter III.

II. SYNTHETIC METHODS

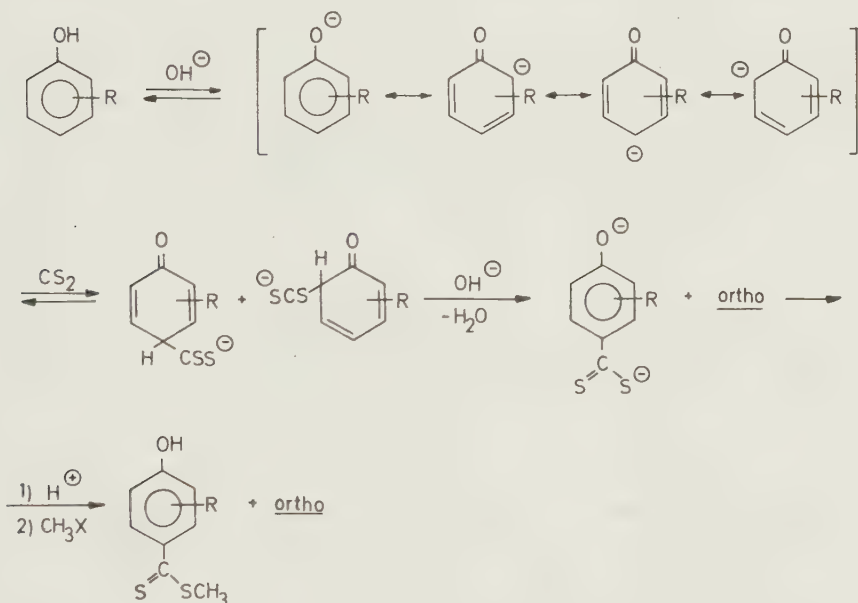
Compounds with the formal structure $X-CH_2-Y$, where X and Y are electron-attracting substituents, react with base and carbon disulphide giving a dithiolate ion. The dianion, on methylation with one or two equivalents of a methylating agent, gives a dithioester derivative or a 1,1-bis(methylthio)ethylene derivative, respectively.



This reaction has been thoroughly investigated by several authors,⁴⁻⁸ and it has been the critical step in the synthesis of most of the compounds investigated in this work.

II.1 Hydroxyaryl-dithioesters

Gompper, Schmidt and Kutter⁴ have synthesized a number of dithiocarbonic acids and esters from phenols and carbon disulphide in a manner analogous to the Kolbe salicyclic acid synthesis.

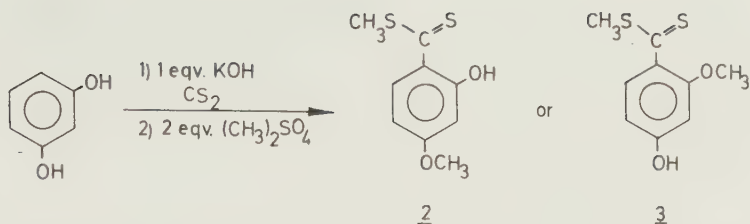


This method has been adapted for the preparation of a series of dithioesters from substituted phenols and naphthols. The compounds prepared are listed in Table I.

Compounds 1, 2, and 4 have previously been prepared by Gompper *et al.*⁴ When resorcinol was treated with base and carbon disulphide, and then with two equivalents of dimethyl sulphate, one compound was isolated (mp 60°) to which they ascribed structure 2.

Table I.

Compound		Yield %	Compound		Yield %
<u>1</u>		82	<u>8</u>		18
<u>2</u>		21	<u>9</u>		25
<u>3</u>		38	<u>10</u>		27
<u>4</u>		43	<u>11</u>		4
<u>5</u>		19	<u>12</u>		61
<u>6</u>		12	<u>13</u>		52
<u>7</u>		60	<u>14</u>		57



However, they gave no proof for this structure, and they also pointed out that it could be the isomer 3. In this investigation the other isomer (mp 126.5–128°) has been obtained from resorcinol monomethyl ether by the same synthetic route. The NMR parameters of 2 and 3 are shown in Table II.

Table II. NMR parameters for 2 and 3.

	Chemical shifts ^a		Coupling constants (Hz)
<u>2</u>	CH ₃ S-	2.65	
	CH ₃ O-	3.78	
	HO-	12.83	
	H ₁	8.13	J _{1,2} = 9.33
	H ₂	6.52	J _{2,3} = 2.70
	H ₃	6.51	J _{1,3} = 0.27
<u>3</u>	CH ₃ S-	2.68	
	CH ₃ O-	3.84	
	HO-	6.50	
	H ₁	7.66	J _{1,2} = 8.59
	H ₂	6.49	J _{2,3} = 2.30
	H ₃	6.53	J _{1,3} = 0.11

^a δ from TMS. Solvent: acetone.

When α -naphthol was treated with base, carbon disulphide and dimethyl sulphate, a reaction mixture was obtained which on analysis with thin layer chromatography (silica, chloroform) gave rise to two yellow spots. After separation on a silica column, two crystalline products (mp 75-77° and 112-113.5°) were isolated. Their elemental analyses and spectroscopic properties showed them to be isomers.

As seen in Table III compounds 2 and 6 exhibit properties that would be expected from intramolecularly hydrogen bonded molecules. Consequently, these compounds have been ascribed the structures with the hydroxy group ortho to the dithioester function. Independent evidence for this assignment in the resorcinol case will be given in the next section.

Table III. Physical data for compounds 2, 3, 5, and 6.

	<u>2</u>	<u>3</u>	<u>5</u>	<u>6</u>
M.p.	60.5-61	126.5-128	112-113.5	75-77
Rf ^a	0.67	0.34	0.39	0.68
IR (ν_{OH}) cm ⁻¹ ^b	2880	3360	3430	2650
NMR (δ_{OH}) ^c	12.83	6.50	5.85	14.20

^a TLC on silica with chloroform as eluent.

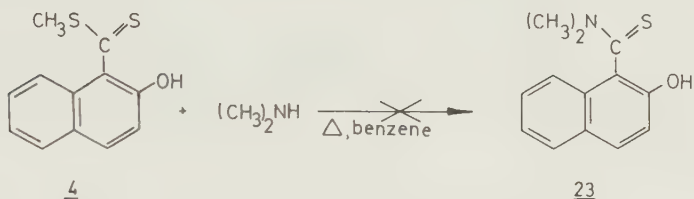
^b In chloroform-d.

^c From TMS in chloroform-d.

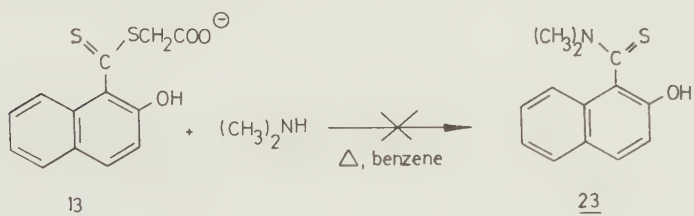
II.2 N,N-Dimethyl-hydroxyaryl-thioamides

Aromatic thioamides containing hydroxy and amino groups can usually not be prepared from the corresponding amide with phosphorous pentasulphide without using protecting groups.⁹ In this investigation, three methods have been found successful, but with varying yields.

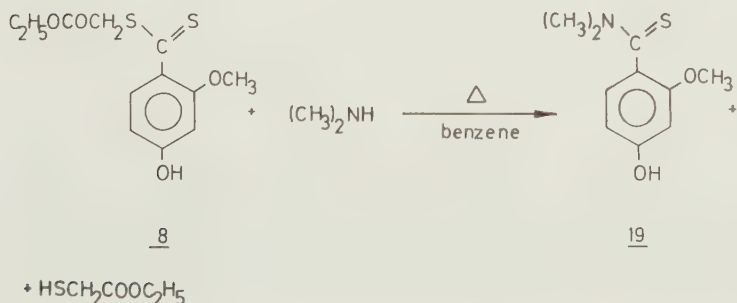
i) Esters of dithio acids are known to give thioamides when treated with amines. Nevertheless, compounds 1 and 4 failed to give thioamides when they were reacted with dimethylamine in boiling benzene. Furthermore the carboxymethyl dithiocarboxy-



lates (e.g. 13) introduced by Holmberg¹⁰ as thioacylating agents, and which have found some use in the preparation of thioamides, did not react under the same conditions. If,



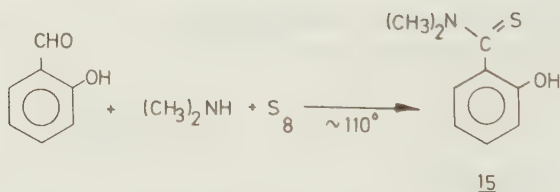
however, the carboxy group is esterified as in 8, the reaction is usually easily carried out.



All dithiobenzoate derivatives and the dithionaphthoate with the dithioester function in the 2-position are completely converted to thioamides within 1-2 hrs in refluxing benzene. The naphthalene derivatives with the dithioester function in position 1 (9 and 10), on the other hand, are noticeably less reactive. 9 was not consumed until after 6 hrs while the isomer 10 still dominated in the reaction mixture after 12 hrs of refluxing. (The course of the reactions was followed by thin layer chromatography.) When the reaction was carried out in a sealed glass tube at 150° all dithioester was consumed overnight.

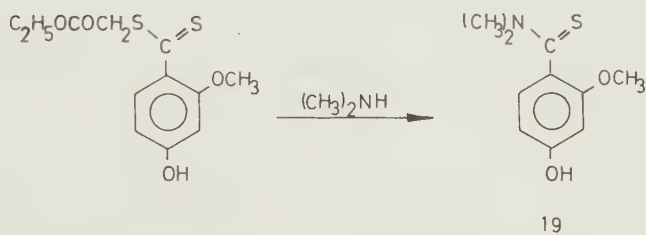
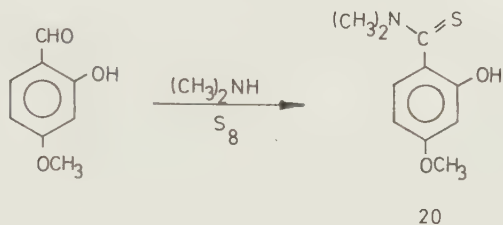
The lesser tendency of these naphthalene derivatives to undergo nucleophilic attack at the thiocarbonyl carbon atom probably has its origin in steric interaction of the peri hydrogen. This exceptional behaviour of 1-substituted naphthalene derivatives has been known for a long time in many reactions, e.g. ester hydrolysis.¹¹ The higher reactivity of 9 might in turn be an effect of intramolecular general acid catalysis.

ii) In the Willgerodt-Kindler¹² reaction, alkyl aryl ketones on treatment with secondary amines and sulphur are converted to ω -aryl thioamides. In a modification¹³ of this reaction, aromatic aldehydes are converted to tertiary thioamides. The method was found applicable to aromatic hydroxyaldehydes such as salicyclic aldehyde as well.



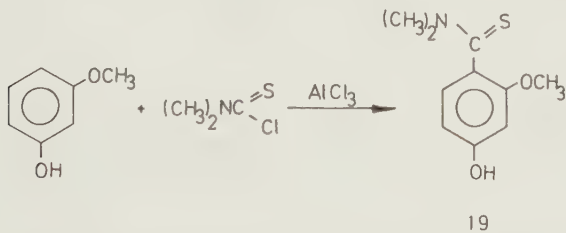
The reaction is normally carried out in boiling morpholine, then used as the amine, but in order to prepare N,N-dimethyl thioamides the aldehydes and sulphur are heated to about 110° and dimethylamine is slowly bubbled through the mixture for about two hrs.

The thioamide obtained from 2-hydroxy-4-methoxy-benzaldehyde by the Willgerodt-Kindler reaction was not identical with the product from the reaction between dithioester 8 and dimethylamine.



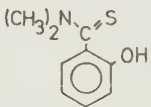
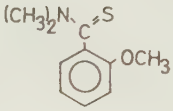
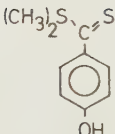
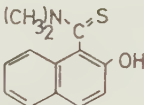
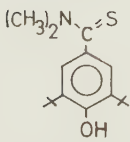
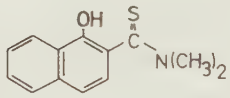
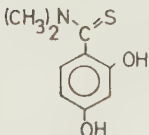
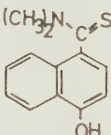
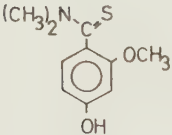
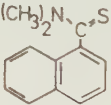
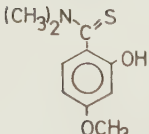
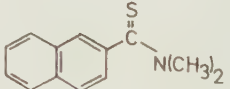
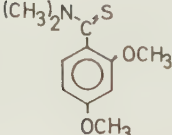
Since 8 was prepared from resorcinolmonomethylether this result is consistent with the structural assignments made in section II.1.

iii) Viola, Scheithauer and Mayer¹⁴ have found that N,N-dimethylthiocarbamyl chloride reacts with activated aromatic compounds in the presence of excess Friedel-Crafts catalysts such as AlCl₃ and SnCl₄ to give N,N-dimethyl thioamides.



The method has been adapted in two cases. From resorcinol monomethylether only 19 could be isolated, but the reaction mixture was complex so that considerable amounts of the

Table IV.

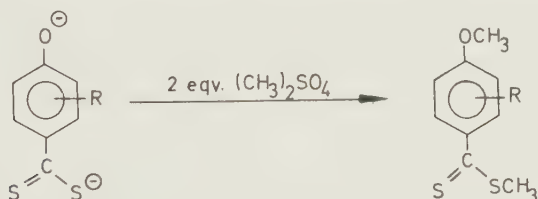
Compound	Method	Yield %	Compound	Method	Yield %
<u>15</u> 	ii	53	<u>22</u> 	iv	57
<u>16</u> 	ii	22	<u>23</u> 	i	58
<u>17</u> 	i	86	<u>24</u> 	i	52
<u>18</u> 	i	84	<u>25</u> 	i	66
<u>19</u> 	i iii	54 45	<u>26</u> 	iv	40
<u>20</u> 	ii	34	<u>27</u> 	iv	21
<u>21</u> 	iii	53			

isomer 20 (see Table IV) might have been formed.

iv) Aromatic thioamides, not containing hydroxy groups, were prepared by thionation of the corresponding amide with phosphorous pentasulphide.

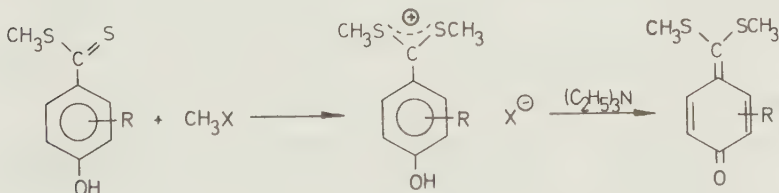
II.3 Quinone methides

Preparation of ω,ω -bis(methylthio)quinone methides through direct methylation of the dithiolate ion with two equivalents of dimethyl sulphate is usually not possible since S,O-alkylation predominates, giving methoxy dithioesters.



If, however, the oxygen atom is sterically hindered or if an alkylating agent that favours an intramolecular S,S-attack, such as ethylene dibromide, is used, the direct alkylation of the dianion is possible.⁴

Alternatively, the para- or ortho-hydroxyaryl dithioesters are alkylated to bis(methylthio)hydroxyaryl carbonium salts which can then be deprotonated by a suitable base.



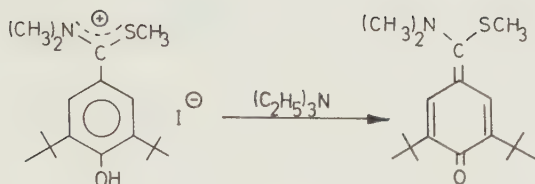
The ω,ω -bis(methylthio)quinone methides are very unstable compounds, and consequently it has generally not been possible to isolate them in pure form. The salts, on the other hand, are reasonably stable and crystalline, and can be

purified by conventional methods and stored for months under dry conditions.

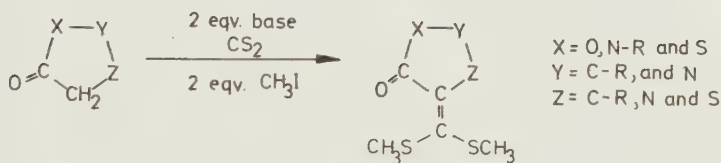
Due to the great reactivity of the quinone methides, the deprotonation step has been carried out directly in the solution used for the spectroscopic experiment. The resulting triethyl ammonium salt is filtered off, and the solution used at once.

ω -Dimethylamino- ω -methylthio-quinone methides should in principle be available by an analogous route. Hydroxyaryl- α -N,N-dimethyl thioamides (see section II.2) are easily methylated on the sulphur atom, for example by methyl iodide. When the reaction is carried out in boiling acetone, pure dimethylamino-methylthio carbonium salt is precipitated in high yields on cooling. Furthermore, the addition of triethylamine to a suspension of the salt in an inert polar solvent, such as acetonitrile, momentarily produces a bright orange- or redcoloured solution.

In this solvent and in other polar solvents such as chloroform, methylene chloride and dry acetone, the triethylammonium salt does not precipitate. The NMR spectrum indicates that the quinone methide is produced, but the spectrum also contains signals from the triethylammonium salt, as well as unidentified signals. If, on the other hand, a less polar solvent such as carbon disulphide or fluorobenzene was used, the solubility of the quinone methide was too low. Despite the use of combinations of several different anions ($I^{\ominus}$, $SO_3OCH_3^{\ominus}$, $BF_4^{\ominus}$, $SO_3F^{\ominus}$), bases (triethylamine, 1,4-diazabicyclo[2,2,2]octane) and solvents (CS_2 , CH_2Cl_2 , $CHCl_3$, C_6H_5F , ortho-dichlorobenzene and acetonitrile), all attempts to prepare pure quinone methide solutions, suitable for variable temperature NMR analysis, were unsuccessful. Attempts to isolate the quinone methides from the solution also failed, with one exception. The evaporated carbon disulphide solution of 2,6-di-*tert*-butyl-quinone methide-[4] gave a product which could be recrystallized from ligroin.



II.4 Azolinones



A modification of the reaction described by Gompper and Töpfl⁵ has proved to be particularly useful. The reaction consists of first mixing the methylene compound, sodium hydride and carbon disulphide in dry benzene followed by the addition of sufficient dimethylformamide to allow the reaction to proceed at a suitable rate. The procedure has been described previously by Sandström and Wennerbeck.¹⁵

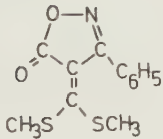
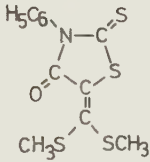
This reaction has been adapted to some oxo derivatives of pyrazolines, oxazolines, isoxazolines and thiazolines and to some rhodanine derivatives. The compounds synthesized are listed in Table V.

If the deprotonation is allowed to take place before carbon disulphide is supplied, the yield decreases. Some other combinations of base and solvent, e.g. sodium hydride in DMSO or sodium ethoxide in abs. ethanol, generally also gave lower yields. The rhodanine derivative 40 was prepared

Table V.

Compound	Yield	Compound	Yield
<u>29</u>	76	<u>35</u>	(9)
<u>30</u>	55	<u>36</u>	39
<u>31</u>	51	<u>37</u>	18
<u>32</u>	62	<u>38</u>	64
<u>33</u>	50	<u>39</u>	40

Table V. cont.

Compound	Yield	Compound	Yield
<u>34</u> 	49	<u>40</u> 	11

by the EtO^-/EtOH method. The poor yield can probably be improved if the reaction is carried out in the NaH/DMF -benzene system.

Attempts to prepare 4-bis(methylthio)methylene-2-phenyl-oxazolin-5-one (35) gave somewhat surprising results. The NMR spectrum of the crude product contained two pairs of singlets in the S-methyl region. Repeated crystallization from ethanol gave pale yellow needles (41) and a more intensely yellow mother liquor which upon evaporation and recrystallization from ligroin ($60\text{--}85^\circ$) gave yellow needles (35). The physical properties of 35 and 41 are shown in Table VI.

Table VI. Physical data for 35 and 41.

	<u>35</u>	<u>41</u>
M.p.	119-120 $^\circ$	144-144.5 $^\circ$
NMR ($\text{CH}_3\text{S-}$) ^a	2.64, 2.89	2.46, 2.70
IR ($\nu_{\text{C=O}}$) ^b	1770	1633
UV (λ_{max} , ϵ) ^c	385 (28 000)	301 (24 800)
	288 (7 180)	231 (11 900)
	2665 (11 640)	

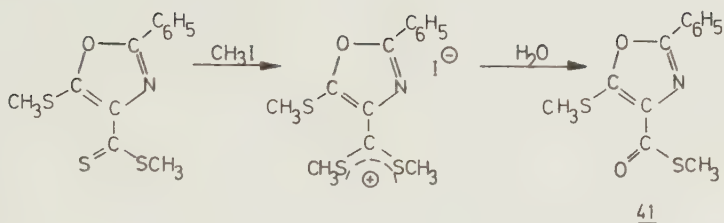
^a From TMS in CDCl_3 .

^b In KBr.

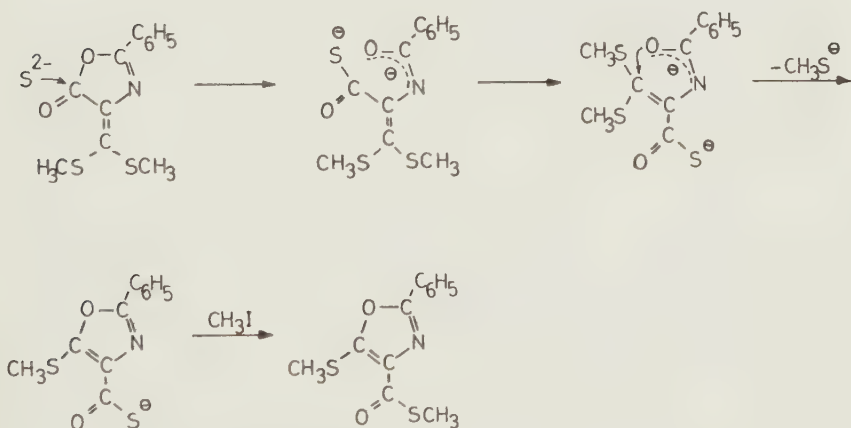
^c In heptane.

Elemental analysis and mass spectroscopy indicated that 35 and 41 were isomers. Brown *et al.*¹⁵ prepared 35 with potassium tert.-butoxide as base in tert.-butanol and DMF, with no mention of the appearance of 41.

Incidentally the same authors¹⁶ have described a compound with the same melting point and spectral properties as 41 obtained from the following reaction:



Obviously the reaction giving 41 from oxazolone, base and carbon disulphide is a rearrangement with a formal inter-change of sulphur and oxygen atoms. A tentative mechanism involving ring opening, rotation around the carbon-nitrogen bond and ring closure may be suggested.

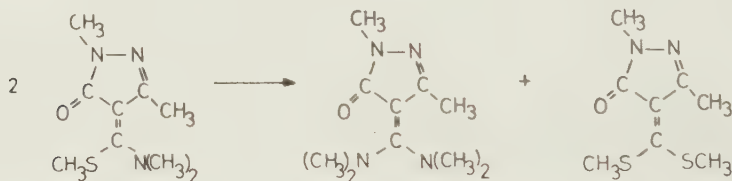


The existence of small amounts of sulphide ions can be detected in reaction mixtures of sodium hydride and carbon disulphide in DMF solutions. The mercaptide ion formed in the reaction may replace the sulphide ion in the primary nucleophilic attack, in which case the methylation step can be excluded.

1,1-Bis(dimethylamino)ethylenes with electron-attracting groups on C-2 have been prepared by Gompper and Töpfl⁵ and by Ericsson, Sandström and Wennerbeck⁶ by the reaction between amines and the corresponding 1,1-bis(methylthio)ethylene. If one equivalent of dimethylamine is used, 1-dimethylamino-1-methylthioethylenes are usually obtained.

When compound 29 was allowed to react with one equivalent of dimethylamine in benzene solution for 20 minutes at room temperature the NMR spectrum of the crude material indicated that the main product was the dimethylamino-methylthio derivative. This was also supported by thin layer chromatography of the reaction mixture. After column chromatography on Al_2O_3 , only 4-bis(dimethylamino)methylene-1,3-dimethylpyrazolin-5-one could be isolated.

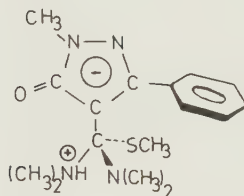
The diamino derivative was probably formed by a disproportionation of the monoamino derivative. However, only traces of 29 could be isolated.



In contrast, 4-bis(methylthio)methylene-1,3-diphenylpyrazolin-5-one (32), with one equivalent of dimethylamine, readily gave the monoamino derivative at room temperature. With excess of dimethylamine 32 gave no diamino derivative even after several hours' boiling.

The small tendency of 32 to produce diamine is probably due to a steric effect of the phenyl group in the 3-position.

If the rate-determining step involves a tetrahedral intermediate, the introduction of a second dimethylamino group goes through a highly strained transition state.



III. METHODS FOR THE EVALUATION OF RATE CONSTANTS FROM NMR SPECTRA

The use of nuclear magnetic resonance lineshape methods in studying intramolecular rate processes has been reviewed by several authors^{1,2,17}. The barrier heights of dynamic processes amenable to this technique extend from activation energies of ca. 25 kcal/mol down to about 5-6 kcal/mol. The work to be described in this thesis deals with exchange processes between two uncoupled sites, A and B, of equal population. For slow exchange the two sites give rise to two signals with different Larmor frequencies. When the rate of exchange is increased, for example by raising the temperature, the signals broaden and approach each other. The temperature at which the minimum between the signals disappears, giving only one broad signal, is denoted the coalescence temperature. At very fast exchange a single sharp line is observed, the frequency of which is the weighted average of the frequencies for the different sites. An example of a spectrum is shown in Fig. 1.

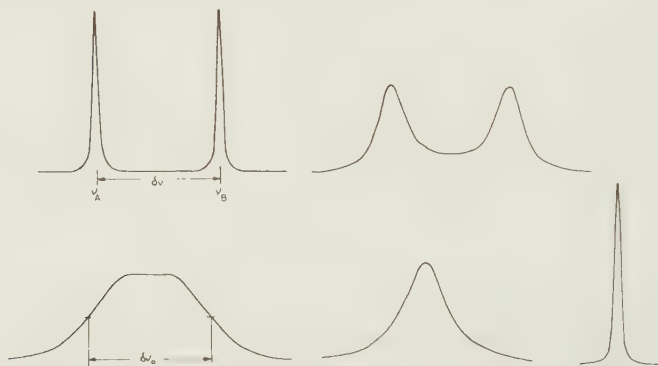


Fig. 1 Temperature dependence of the NMR spectrum.
(Two equally populated, uncoupled sites.)

The shape of a resonance signal is described by means of a set of classical equations derived by Block.¹⁸ The effects of exchange processes upon the NMR spectrum is described by these equations modified by Hahn and Maxwell¹⁹ and McConnell²⁰. The measured absorption intensity at a frequency ν is proportional to the imaginary component of G , given by the line-shape equation:

$$G = u + iv = -iC \frac{[\tau_A + \tau_B + \tau_A \tau_B (\alpha_A p_B + \alpha_B p_A)]}{(1 + \alpha_A \tau_A) (1 + \alpha_B \tau_B) - 1} \quad (1)$$

In this equation,

$$C = \gamma H_1 M_0$$

τ_A and τ_B = the mean lifetimes in sites A and B

p_A and p_B = the populations in sites A and B

$$\alpha_A = \frac{1}{T_{2A}} - 2\pi i (\nu_A - \nu)$$

$$\alpha_B = \frac{1}{T_{2B}} - 2\pi i (\nu_B - \nu)$$

$T_2 = T_{2A} = T_{2B}$ = the transverse relaxation time

The imaginary part of the equation is:

$$\text{Im } (G) = -C \frac{\{P[1 + \tau(p_B/T_{2A} + p_A/T_{2B})] + QR\}}{P^2 + R^2} \quad (2)$$

where

$$\tau = p_B \tau_A = p_A \tau_B$$

$$P = \tau \left[\frac{1}{T_{2A} T_{2B}} - 4\pi^2 \Delta\nu^2 + \pi^2 \delta\nu^2 \right] + \frac{p_B}{T_{2B}} + \frac{p_A}{T_{2A}}$$

$$Q = \tau [2\pi \Delta\nu - \pi \delta\nu (p_A - p_B)]$$

$$R = 2\pi\Delta\nu[1 + \tau(1/T_{2A} + 1/T_{2B})] + \pi\delta\nu\tau(1/T_{2B} - 1/T_{2A}) + \pi\delta\nu(p_A - p_B)$$

$$\Delta\nu = 1/2 (\nu_A + \nu_B) - \nu$$

$$\delta\nu = \nu_A - \nu_B$$

If the population is equal in the two sites, that is

$$p_A = p_B = 1/2 \quad \text{then}$$

$$\tau = p_B\tau_A = p_A\tau_B = 1/2 \tau_{A(B)}$$

and a simplified equation is obtained:²⁰

$$G = u + iv = \frac{-iC\tau[2 + (T_2^{-1} + 2\pi i\nu)\tau]}{\tau^2[T_2^{-1} + \tau^{-1} - 2\pi i(\nu_A - \nu)][T_2^{-1} + \tau^{-1} + 2\pi i(\nu_A - \nu_B)]} \quad (3)$$

Equation (3) allows computation of spectra for appropriate input values of τ_A , τ_B , ν_A , ν_B , p_A , p_B , T_{2A} and T_{2B} . For comparison of the theoretical and experimental lineshapes a computer program was used which changes the variable parameters until the best fit is obtained by means of the STEPIT procedure.²¹

The parameter $\delta\nu$ is allowed to vary at temperatures below coalescence and then extrapolated from the low temperature data to obtain values at higher temperatures.

The transverse relaxation time T_2 is given by the equation:

$$T_2 = \frac{1}{\pi\Delta\nu_{1/2}} \quad (4)$$

where $\Delta\nu_{1/2}$ is the signal linewidth at half maximum intensity in the absence of exchange. Thus, T_2 can not be measured

directly in the region of intermediate exchange, nor can it be varied by the program until best fit is obtained, since T_2 and τ are covariant. Instead, T_2 has been determined by monitoring the linewidth W'_{ref} of a reference signal, for example TMS, at each temperature, and the linewidth of the exchanging signal W_1 at a temperature below the region where exchange broadening is noticeable. At this temperature the linewidth of the reference signal is W_{ref} and T_2 at each temperature is obtained from the formula:

$$T_2 = \frac{1}{\pi(W_1 + W'_{\text{ref}} - W_{\text{ref}})} \quad (5)$$

which is derived under the assumption that the linewidths of both signals are equally affected by homogeneity and viscosity changes.

The rate constant, k , is related to τ by the relation:

$$k = \frac{1}{2\tau} ; \quad (p_A = p_B = 0.5) \quad (6)$$

The free energy of activation is obtained from the Eyring equation:

$$\Delta G_T^* = - 2.303 RT \log \frac{hk}{k_B T \kappa} \quad (7)$$

where k_B = Boltzmann's constant

h = Planck's constant

κ = transmission coefficient, assumed to be unity

From equation (6) and the thermodynamic relation

$$\Delta G^* = \Delta H^* - T\Delta S^* \quad (8)$$

the enthalpy of activation, $\Delta H^\ddagger$ and the entropy of activation, $\Delta S^\ddagger$ are obtained by plotting $\log \frac{k}{T}$ against $1/T$. The equation is of the form:

$$\log \frac{k}{T} = - \frac{\Delta H^\ddagger \log e}{RT} + \frac{\Delta S^\ddagger \log e}{R} + \log \frac{k_B}{h} \quad (9)$$

At the coalescence temperature, the exchange rate k_c is given by the equation:²²

$$k_c = \frac{\pi(\nu_A - \nu_B)}{\sqrt{2}} \quad (10)$$

The use of this approximation to obtain free energy barriers at the coalescence temperature is very widespread, and there is little doubt that the $\Delta G^\ddagger$ values thus obtained for 2-site cases are relatively free from error.²³

Temperature measurements

The measurement of temperature was carried out by determining the peak separation between two signals with a temperature-dependent internal chemical shift. The mixture in question was kept in a capillary which was centered in the NMR tube by means of two Teflon plugs. The capillaries were calibrated against a copper constantan thermocouple over the whole temperature interval in which they were used, a procedure previously described.²⁴ This method can be estimated to ensure an accuracy of ca. $\pm 1^\circ\text{C}$. Of more importance for the determination of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values is, however, the accuracy of the relative temperature differences within each set of spectra recorded. In this sense the accuracy is considerably better, ca. $\pm 0.3^\circ\text{C}$.

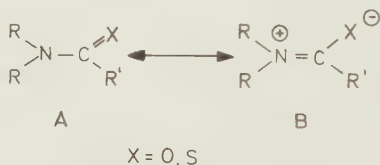
Four different solutions were used: a) neat methanol, b) methylene chloride, methanol- d_3 and hydrochloric acid, c) β -picoline and water, d) ethylene glycol.

In each experiment a capillary covering the temperature interval of interest was chosen. In addition, the choice of capillary was made so that the temperature-dependent signals and the exchanging signals did not overlap.

IV. HYDROXY AND METHOXY SUBSTITUTED AROMATIC THIOAMIDES

IV.1 Introduction

Amides and thioamides have been extensively studied in order to obtain information about the barrier to internal rotation around the carbon-nitrogen bond. The polar form of the resonance notation suggests that the carbon-nitrogen bond should have partial double bond character, and that rotation about this bond should be more hindered than about a carbon-nitrogen bond not participating in a conjugated system.



This prediction was confirmed experimentally in 1956 when the barrier ($\Delta G^\ddagger$) in N,N-dimethylformamide was found to be ca. 22 kcal/mol.²² Since then the barriers of many amide systems have been determined.¹⁷

Replacement of the carbonyl oxygen atom of an amide by a sulphur atom results in a significant increase in the rotational barrier. Thus the barrier in N,N-dimethylthioformamide was found to be ca. 24 kcal/mol.²⁵ The barrier in N,N-dimethylthiobenzamide is known from studies by Sandström²⁶ to be 18.4 kcal/mol, that is about 6 kcal/mol lower than the barrier in N,N-dimethylthioformamide. The observed lowering of the barrier has been attributed to electronic effects; competitive conjugation is believed to decrease the transition state energy more than the ground state energy. The same trend is observed in the analogous amide systems. However, it has been shown that the angle between the thioamide plane and the benzene ring is ca. 40 degrees²⁷⁻²⁹, indicating that steric interaction in the initial state is considerable. Introduction of one ortho substituent in benzamides and thiobenzamides usually produces a noticeable effect on the barrier height. No systematic, quantitative investigation has been carried out,

but the barrier height turns out to be determined primarily by the steric demands of the substituent and not so much by its electronic effects. Thus, introduction of the substituents Cl, NO₂, Me and OMe all causes an increase in barrier height in N,N-dibenzylbenzamide.³⁰ Severe steric interaction raises the barrier in N-methyl-N-benzyl-2,4,6-tri-tert.-butylbenzamide to over 30 kcal/mol.³¹

In ortho-chloro-N,N-diethylbenzamide Bedford *et al.*³² reported magnetic non-equivalence of the geminal methylene hydrogens at low temperature. These authors attributed the non-equivalence to unequal populations of the three rotameric conformations of the methylene group, due to steric interference of the ethyl group with the ortho substituent. Siddall and Garner,³³ on the other hand, explained this phenomenon by slow rotation around the phenyl-carbonyl bond. Lewin and Frucht³⁰ found that the methylene signals in ortho substituted N,N-dibenzylbenzamides gave rise to two AB quartets at low temperatures (usually 0°C and below). In symmetrically 2,6-disubstituted benzamides, the non-equivalence of the methylene proton disappeared while, in contrast, unsymmetrically ortho disubstituted N,N-dibenzylbenzamides resembled the benzamides with one ortho substituent. These observations clearly support the proposal of Siddall and Garner.

Lewin and Frucht³⁰ also mention that ortho-hydroxy- and ortho-amino substitution causes a decrease in the barrier for rotation around the carbon-nitrogen bond and, in addition, prevents the occurrence of a chiral center because of the formation of a six-membered cyclic chelate. No quantitative data are presented in this investigation.

The aim of the present investigation is to study the effects of hydroxy and methoxy substitution in the ortho and para positions in N,N-dimethylthiobenzamides and N,N-dimethylthionaphthamides on the torsional barrier around the carbon-nitrogen bond. Special attention has been devoted to the effects of intra- and intermolecular hydrogen bonding and of steric interference. Interesting information can also be expected from infrared spectra of these compounds, particularly concerning the strength and concentration dependence of hydrogen bonding.

The ultraviolet spectra of thiobenzamides are known to be strongly dependent on the angle between the thioamide group and the benzene ring. Departure from coplanarity results in hypsochromic shifts of the $\pi \rightarrow \pi^*$ band. Since ortho substitution affects the angle around the pivot bond, the compounds under this consideration are expected to show changes in the position of this band. Moreover, the position and the intensity of the long wavelength, $n \rightarrow \pi^*$ band are sensitive to both steric effects and hydrogen bonding.

IV.2 Results of barrier measurements

The free energies of activation at the coalescence temperature for the thiobenzamides and the thionaphthamides, calculated by the approximate equation (10), are summarized in Tables VII and VIII. As the coalescence temperatures range from - 16 to + 186°C and as an attempt has been to use the same solvent for all compounds, the number of alternative solvents is highly reduced. With two exceptions, all of the spectra were recorded in ortho-dichlorobenzene (ODC). This is a reasonably inert solvent with a comparatively low tendency to form hydrogen bonds,³⁴ a condition of great importance for the present systems. Furthermore, ODC has been widely used for barrier measurements of amides and thioamides. The low solubility of compound 16 in ODC made it necessary to use another solvent. Thus 16 has been studied in dimethyl sulphoxide. The likewise para-hydroxy substituted compounds 19 and 25 also demonstrated low solubility in ODC at moderate temperatures, but because of the much higher coalescence temperature of these compounds, their solubility in a temperature interval relevant for the measurement was acceptable. Some of the substances were studied in more than one solvent. No significant difference in $\Delta G^\ddagger$ was obtained for deuteriochloroform, ODC and even DMSO, despite the possibility of the latter solvent to form strong hydrogen bonds with phenols.³⁵ On the other hand, a drastic change in barrier was observed for N,N-dimethyl-2-hydroxy-4-methoxy-thiobenzamide in pyridine-d₅,

Table VII. Coalescence data for N,N-dimethylthiobenzamides.

	Compound	Solvent	$\delta\nu$ Hz	T_c K	$\Delta G_{T_c}^\ddagger$ kcal/mol
<u>15</u>		ODC	25.5	302.5	15.3
<u>16</u>		$(CD_3)_2SO$	19.4	343.6	17.6
<u>17</u>		ODC	24.4	331.1	16.8
<u>22</u>		ODC	32.3	440.0	22.4
<u>28</u>		ODC	26.2	335.3	17.0
<u>20</u>		$CDCl_3$	13.9	258.7	13.3
		pyridine- d_5	19.0	298.1	15.2
<u>19</u>		ODC	31.1	431.2	21.9
		$(CD_3)_2SO$	27.4	428.9	21.9

Table VII. cont.

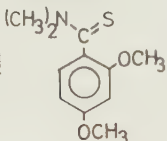
Compound	Solvent	$\delta\nu$ Hz	T_c K	$\Delta G_{T_c}^*$ kcal/mol
$\underline{21}$ 	ODC	30.6	419.5	21.3

Table VIII. Coalescence data for N,N-dimethylthionaphthamides.

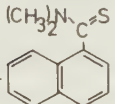
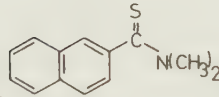
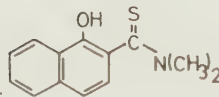
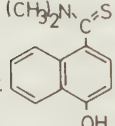
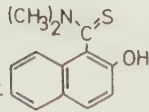
Compound	Solvent	$\delta\nu$ Hz	T_c K	$\Delta G_{T_c}^*$ kcal/mol
$\underline{26}$ 	ODC	51.5	458.9	22.9
$\underline{27}$ 	ODC	34.2	358.7	18.0
$\underline{24}$ 	ODC + C ₆ H ₅ F	26.8	258.1	12.9
	CDCl ₃	21.3	256.7	13.0
$\underline{25}$ 	ODC	48.4	441.0	22.1
	(CD ₃) ₂ SO	41.2	438.7	22.1
$\underline{23}$ 	ODC	48.5	405.6	20.2

Table IX. Results from the complete lineshape treatment of
20 in ortho-dichlorobenzene and fluorobenzene (3:1).

T K	$\delta\nu$ Hz	T_2 sec	τ sec	$\Delta G^\ddagger$ kcal/mol
248.1	17.4	0.152	0.129	13.4
250.1	17.5	0.177	0.0949	13.4
252.2	17.6	0.212	0.0712	13.4
253.2	17.6	0.168	0.0763	13.4
254.4	17.8	0.168	0.0546	13.3
257.4	17.8	0.177	0.0497	13.4
260.4	18.0	0.212	0.0367	13.4
263.5	18.1	0.212	0.0208	13.3
264.2	18.2	0.227	0.0202	13.3
267.1	18.3	0.245	0.0144	13.3
269.3	18.4	0.265	0.0125	13.4
269.4	18.4	0.265	0.0119	13.3
271.3	18.5	0.318	0.0122	13.4

Table X. Results from the complete lineshape treatment of 24 in deuteriochloroform.

T K	$\delta\nu$ Hz	T_2 sec	τ sec	$\Delta G^\ddagger$ kcal/mol
243.6	19.6	0.398	0.0821	13.0
245.7	19.8	0.490	0.0625	12.9
246.9	19.8	0.430	0.0584	13.0
249.6	19.7	0.448	0.0439	13.0
250.2	20.0	0.426	0.0383	12.9
251.9	19.9	0.430	0.0342	13.0
252.2	20.0	0.461	0.0334	13.0
253.8	19.8	0.430	0.0286	13.0
256.3	20.0	0.455	0.0217	13.0
259.5	20.1	0.448	0.0162	13.0
260.9	20.1	0.430	0.0145	13.0
263.6	20.2	0.468	0.0107	13.0
266.5	20.2	0.455	0.00844	13.0
269.0	20.3	0.448	0.00641	13.0

Table XI. Thermodynamic parameters for 20 and 24 obtained from the complete lineshape analyses.

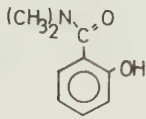
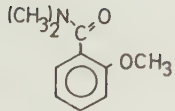
Compound	$\Delta H^\ddagger$ kcal/mol	$\Delta S^\ddagger$ cal/mol K
<u>20</u>	13.6 ± 0.5	0.9 ± 1.8
<u>24</u>	12.3 ± 0.1	-2.5 ± 0.5

indicating that this solvent is able to form strong hydrogen bonds to the solute.

A complete lineshape analysis for the N-methyl signals was performed for two compounds, 20 and 24. These two compounds show barriers much lower than usual for ordinary aromatic N,N-dimethylthioamides. For 20 ODC containing 25 % fluorobenzene was chosen as solvent, in order to make possible a direct comparison with the approximately obtained $\Delta G^\ddagger$ values. The low effective T_2 values at low temperatures, probably have their origin in high viscosity of the solution. For 24, deuteriochloroform was chosen as solvent. The methoxy signal in 20 and TMS for 24 were used as reference signals for determination of the transverse relaxation times T_2 . The results from the complete lineshape analyses are summarized in Table IX and X, and the activation parameters obtained from the Eyring plots are shown in Table XI.

For comparison, coalescence data of N,N-dimethyl-2-hydroxybenzamide (49) have also been measured. 49 was not sufficiently soluble in ortho-dichlorobenzene and was therefore studied in deuteriochloroform. The results are collected in Table XII.

Table XII. NMR parameters and $\Delta G^\ddagger$ values for 49 and 50

Compound	Solvent	$\delta\nu$ Hz	T_c K	$\Delta G^\ddagger$ kcal/mol
<u>49</u> 	CDCl ₃	8.8	264.4	13.9
<u>50</u> 	ODC	17.2	354.9	18.3

IV.3 Infrared and NMR data on hydrogen bonding

One important factor in the understanding of the low barriers of the ortho-hydroxy-N,N-dimethylthiobenzamides is the existence and strength of hydrogen bonds in these compounds. Likewise, hydrogen bonding in the para-hydroxy-N,N-dimethylthiobenzamides can affect their barriers.

Infrared spectroscopy provides the most commonly used criterion for the presence of hydrogen bonding. The stretching mode of the O-H bond is shifted to lower frequency by hydrogen bond formation and the frequency shift has been proposed³⁶ to be linearly related to the hydrogen bond energies, $-\Delta H$. There has been some controversy concerning this relationship, but it turns out that the linear correlation holds for minor structural changes in the basic and acidic species.³⁷ Infrared data for ortho- and para-hydroxythiobenzamides and thionaphthamides are shown in Table XIII. In addition, the table contains data for three analogous dithioesters.

The concentration dependence of the intensity ratio between the bands of free and associated forms was also studied. The para-hydroxy substituted derivatives, except 17, showed a concentration dependence typical for intermolecularly hydrogen bonded systems. Upon dilution, the relative intensity of the sharp band assigned to unassociated OH-stretching band increased at the expense of the intensity of the broad band at lower frequency assigned to the associated form. On the other hand, the ortho-hydroxy substituted derivatives exhibited no concentration dependence. One exception was 23, which showed a concentration dependence of the intensity ratio (Fig. 2).

¹H NMR signals are shifted downfield on hydrogen bonding. Although there is a large number of contributions to the chemical shift change accompanying interactions such as hydrogen bonding, and it is unlikely that the hydrogen-bonding contribution can be separated from the other terms, the position of the phenolic hydroxy proton chemical shifts has been found to be linearly related to $-\Delta H$ in a series of 30 phenol-base systems.³⁵ The chemical shifts for the hydroxy protons of the thioamides and the corresponding dithioesters

Table XIII. Infrared data for thioamides and dithioesters^a.

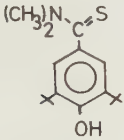
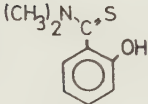
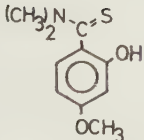
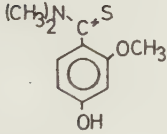
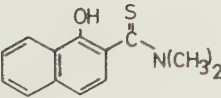
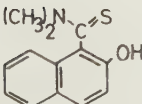
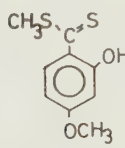
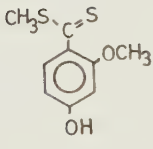
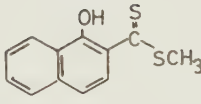
Compound	$\nu_{\text{OH free}}(\text{cm}^{-1})$	$\nu_{\text{OH complexed}}(\text{cm}^{-1})$	$\Delta\nu_{\text{OH}}(\text{cm}^{-1})$
<u>17</u> 	3630	-	-
<u>15</u> 	3590	3250	340
<u>20</u> 	3590	3140	450
<u>19</u> 	3590	3200	390
<u>24</u> 	3580	3130	450
<u>23</u> 	3585	3310	275

Table XIII. cont.

Compound	$\nu_{\text{OH free}}(\text{cm}^{-1})$	$\nu_{\text{OH complexed}}(\text{cm}^{-1})$	$\Delta\nu_{\text{OH}}(\text{cm}^{-1})$
<u>2</u>  <chem>COc1ccc(cc1)C(=S)SC</chem>	-	2880	(700)
<u>3</u>  <chem>COc1ccc(cc1)C(=S)SC</chem>	3580 ^b	3360	220
<u>6</u>  <chem>Cc1ccc2ccccc2c1C(=S)SC</chem>	-	2650	(930)

^a 5 % in CDCl_3 . Cell thickness: 0.1 mm. 25°C.

^b ca. 3 % (saturated solution) in CDCl_3 .

Table XIV. Chemical shifts for OH protons.

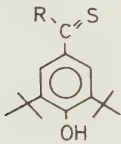
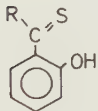
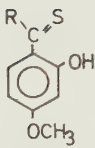
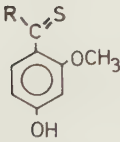
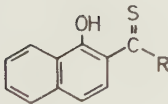
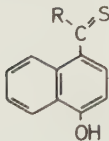
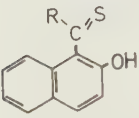
Compound	δ ppm ^a	
	R = CH ₃ S-	R = (CH ₃) ₂ N-
	5.83 ^b	5.25
	-	7.20
	12.83	9.20
	6.50	8.30
	14.20	9.42
	5.85	- ^c

Table XIV. cont.

Compound	δ ppm ^a	
	R = CH ₃ S-	R = (CH ₃) ₂ N-
	6.62	7.20

^a Relative to TMS in CDCl₃.

^b R = C₆H₅CH₂S-

^c The signal is hidden in the multiplet of the aromatic protons.

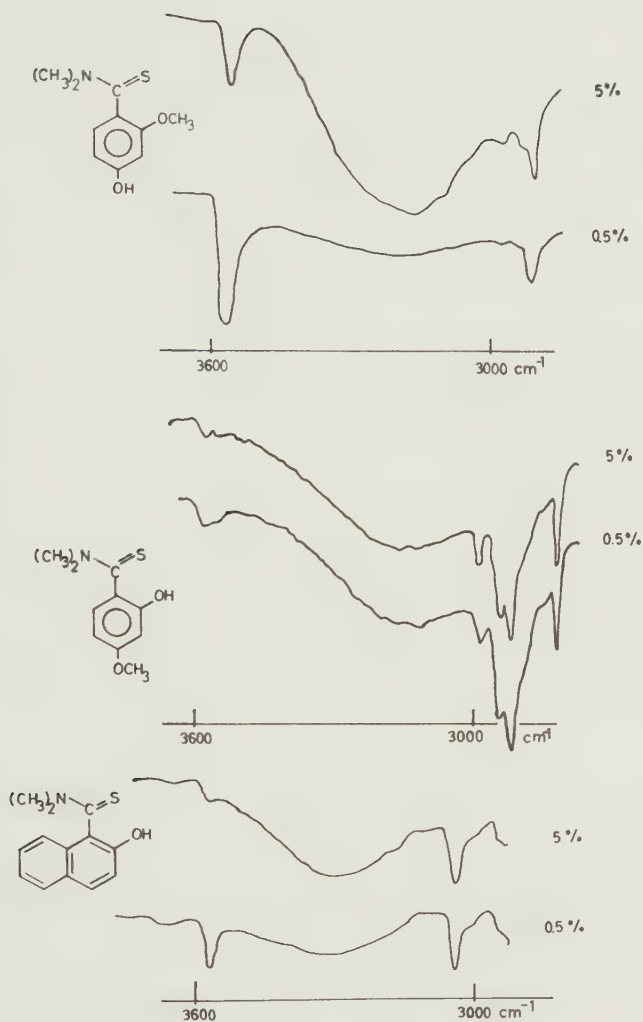


Fig. 2 Infrared spectra of compounds 19 (top), 20 (middle) and 23 (bottom) in CDCl_3 solutions.

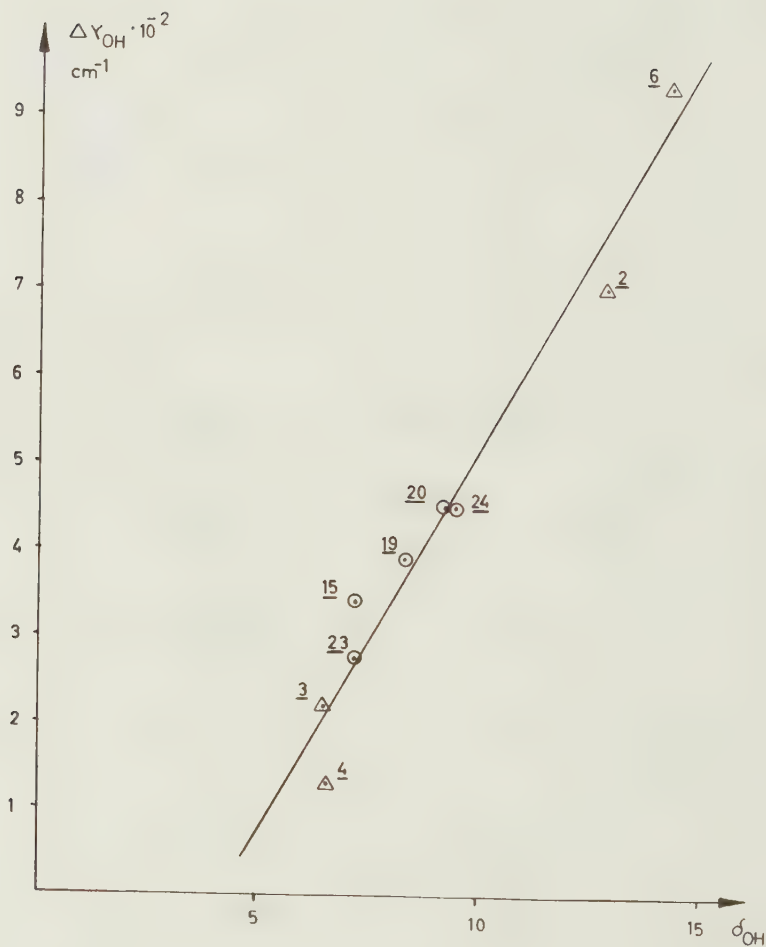


Fig. 3 $\Delta\nu_{OH}$ vs. NMR chemical shifts for the phenolic protons in CDCl_3 solutions.

in about 10 percent deuteriochloroform solutions are summarized in Table XIV.

Fig. 3 shows the correlation between $\Delta\nu_{\text{OH}}$ and the chemical shift. The infrared and NMR results make it possible to determine whether the compounds in question are intra- or intermolecularly hydrogen bonded and to estimate the strength of the hydrogen bond. Thus the two dithioesters 2 and 6 are obviously intramolecularly hydrogen bonded by strong bonds. The analogous thioamides 20 and 24 and compound 15 are likewise intramolecularly hydrogen bonded but with much weaker bonds.

Both the dithioesters and the thioamides with a hydroxy group in the para position are intermolecularly hydrogen bonded, but the bonds are stronger in the thioamide series than in the dithioester series, in contrast to the ortho-hydroxy derivatives.

The two tert.-butyl groups in 17 effectively make any hydrogen bond impossible.

The anomalous behavior of 23 probably has its origin in a steric effect as well. The peri-hydrogen forces the thioamide group out of the plane of the naphthalene ring, thus removing the sulphur atom from the region where intramolecular hydrogen bonding is possible.

IV.4 Discussion of the barriers

Certain generalizations emerge from the results of the barrier measurements:

- 1) Introduction of a hydroxy group in the ortho position lowers the barrier by 3-5 kcal/mol.
- 2) Introduction of a methoxy group in the ortho position raises the barrier by 3-5 kcal/mol.
- 3) Introduction of a hydroxy group or a methoxy group in the para position lowers the barrier by 0.5-2 kcal/mol.
- 4) The barrier in N,N-dimethyl-1-thionaphthamide is almost 5 kcal/mol higher than in the 2-substituted isomer.
- 5) The same trends are observed in the amide series as in

the thioamide series, but the effects are less pronounced.

6) The influence of the solvent on barrier heights is small, except for the ortho-hydroxy substituted derivatives in basic solvents such as pyridine, in which the intramolecular hydrogen bond is broken.

Since amides and thioamides are believed to coordinate with the oxygen and sulphur atoms on hydrogen bonding to protic species, the torsional barriers of such compounds are expected to be higher in protic solvents than in other solutions. Hydrogen bonding may stabilize the polar structure B more than A (page 32) and thus increase the double bond character of the carbon-nitrogen bond. This has been found to be the case for amides dissolved in protic solvents (e.g. water³⁸ and formamide³⁹).

The effect of added phenol on the rate of rotation around the carbonyl-nitrogen bond in N-methyl-N-benzyl-2-chlorobenzamide and in its thio analog in ortho-dichlorobenzene has been studied by Siddall *et al.*³⁴ They found that $\Delta G^\ddagger$ increased with phenol concentration, whereas $\Delta S^\ddagger$ never deviated significantly from zero. The effect of phenol on the thioamide barrier was however much less marked and close to the experimental error.

Sandström²⁶ has investigated the influence of the solvent on the barrier in methyl N,N-dimethyldithiocarbamate and found that the $\Delta G^\ddagger$ value was almost the same in carbon tetrachloride, o-dichlorobenzene, chloroform and 2-propanol. This lesser tendency of the thioamide barriers to be affected by protic solvents is consistent with the weaker association of thioamides with protic species.³⁷

Instead of raising the barrier, introduction of an ortho-hydroxy group has the opposite effect and it is obvious that we must seek another model for the rotational process in these systems.

The barrier heights in these compounds can be discussed in terms of four variables, and the effect of each variable on the rotational barrier is mutually dependent on the others. Furthermore, this dependence does not have to be the same in the initial state as in the transition state. The four

variables are:

- 1) The angle between the amino group and the thiocarbonyl group (θ) and the planarity contra the pyramidalicity around the nitrogen atom.
- 2) The angle between the benzene ring and the thiocarbonyl group (φ).
- 3) The steric interference between the E-methyl group* and the ortho-hydrogen.
- 4) The effect of the intramolecular hydrogen bond.

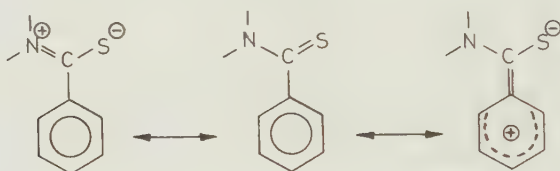
1) From all available results, e.g. X-ray data, it follows that the key atoms of the undisturbed thioamide group are situated in a plane in the same way as the ligands at normal olefinic double bonds. This means that the angle between the amino group and the thiocarbonyl group (θ) is zero and that the dimethylamino group is planar in the initial state of the rotation. The stiffness of the thioamide group is illustrated by the high torsional barrier of dimethylthioformamide (24 kcal/mol).²⁵ However, a steric strain may make the planar conformation impossible. Such a strain could be relieved either by a rotation of the dimethylamino group out of the plane or by a pyramidalization at the nitrogen atom.

In the transition state the dimethylamino group is believed to be twisted 90 degrees, thus inhibiting its conjugation with the thiocarbonyl group, whereas it is uncertain whether the dimethylamino group is planar or pyramidal. If the steric strain operates only in the initial state and raises its energy, it will lower the barrier.

2) The angle between the benzene ring and the thiocarbonyl group (φ) is of great importance for the barrier height. If this angle is zero, maximum conjugation between the ring and the thiocarbonyl group is obtained. In N,N-dimethylthiobenzamide this angle has been shown to be ca. 40 degrees²⁷⁻²⁹ due

* Terminology according to Ref. 40.

to steric interaction between the nearest methyl group and the ortho-hydrogen (vide infra). This angle is however not necessarily the same in the transition state as in the initial state. In the transition state, the interfering methyl group is twisted out of the region in which steric interaction can be expected. The rotation can thus be coupled with a decrease of the angle φ , resulting in more effective conjugation between this group and the benzene ring with accompanying gain in delocalization energy. Moreover, this energy gain is larger in the transition state than in the initial state, since in the transition state the cross conjugation with the dimethylamino group is inhibited.



The π -barrier accompanying rotation around the benzene-thio-carbonyl bond is of course also affected by substitution in the ring. This effect will change the energy of the transition state relative to that of the initial state.

3) As pointed out previously, steric interference between the E-methyl group and the ortho-hydrogen prevents a planar conformation in the initial state²⁷⁻²⁹ (Fig. 4). In the transition state this interaction is eliminated.

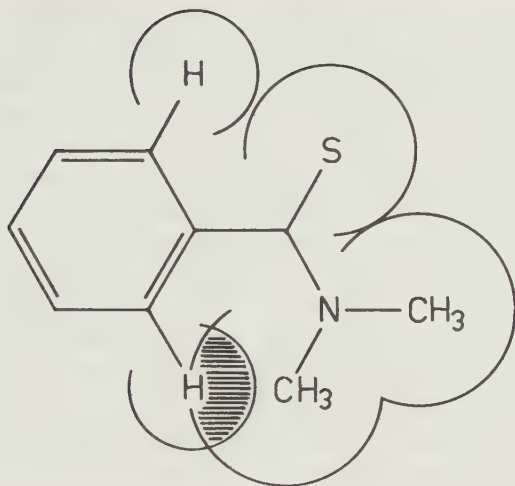


Fig. 4 Steric interference in N,N-dimethylthiobenzamide. 0.75 of the van der Waals radii have been chosen as reasonable values.

4) In the ortho-hydroxy-thiobenzamide derivatives, a moderately strong intramolecular hydrogen bond was experimentally verified. The strength of this hydrogen bond is dependent on all the variables discussed in 1) - 3). According to the simple electrostatic model of the hydrogen bond proposed by Pauling,⁴¹ maximum strength of the bond is obtained with a planar thioamide since then the negative charge on the sulphur atom is largest.

The energy of the hydrogen bond also depends on the distance between the sulphur atom and the oxygen atom, and thus the angle φ , the ideal distance for hydrogen bonding being the situation where this angle is zero or near zero.

Due to the steric interference discussed above, both the angles θ and φ cannot be zero simultaneously. If the sulphur atom through hydrogen bonding is forced nearer the plane of the ring, the dimethylamino group has to be twisted or pyramidalized. However, it seems unlikely that the sulphur

atom lies in the benzene planes in the ortho-hydroxy substituted N,N-dimethyl-thiobenzamides for the following reason.

It has been observed⁴² that in secondary ortho-hydroxy thiobenzamides, where the single substituent on nitrogen is in the Z position and consequently the sulphur atom may lie in the plane, the NMR signal of the ortho-hydrogen is shifted 0.5-1 ppm to lower field compared to the signals of the other aromatic protons. Such a downfield shift is not observed in N,N-dimethylthiobenzamide nor in the ortho-hydroxy derivatives. A comparison with the dithioesters 2 and 3 is interesting. A strongly deshielding region in the plane of the thiocarbonyl function makes the ortho-hydrogen shift to lower field if the sulphur atom lies in the plane of the ring. The hydrogen atom moves out of the deshielding region if the thiocarbonyl group is forced out of the plane as in 3.

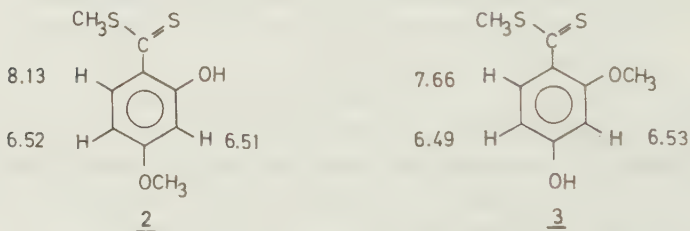


Fig. 55 Chemical shifts (δ) for the ring protons in ppm from TMS (solvent: acetone).

The fact that the ring hydrogen atom in the ortho-position in ortho-hydroxy substituted N,N-dimethylthiobenzamides is not shifted downfield supports the suggestion that the sulphur atom does not lie in the benzene plane. Moreover, the distance between the sulphur and oxygen atoms becomes greater when the thiocarbonyl group is twisted, which is consistent with the observed weaker hydrogen bonds in the ortho-hydroxy substituted thioamides compared to that in the corresponding dithioesters.

Thus, in the initial state for the rotation both the angles θ and ϕ are larger than zero. The magnitudes of these

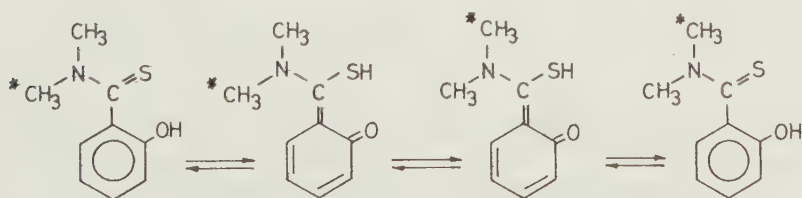
angles are determined by the maximum energy gain obtained by resonance and hydrogen bonding, balanced by the steric interaction between the E-methyl and the ortho-hydrogen. The overall result must be a lower energy compared to a situation with no hydrogen bond.

In the transition state, the sulphur atom can move still nearer the ideal distance for hydrogen bonding, that is in the plane of the ring. The strength of an eventual hydrogen bond in the transition state can of course not be studied experimentally.

Bearing in mind the barrier lowering effect of the introduction of a hydroxy group in the ortho-position, it appears that the energy of the transition state should be lowered more than that of the initial state, *i.e.* the hydrogen bond should be stronger in the transition state than in the initial state. It is believed that this is the main reason for the barrier lowering effect of ortho-hydroxy substitution.

Theoretically, in the state with $\theta = 90^\circ$ a hydrogen bond can be formed to the nitrogen atom instead, as in this case the lone pair electrons are localized. This alternative is, however, less attractive since the only path to this configuration is through a state in which both the angles θ and ϕ are large, *i.e.* a state of high energy.

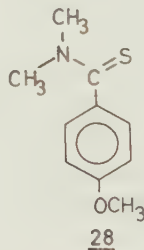
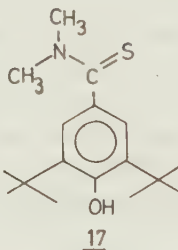
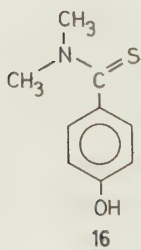
Another mechanism for the rotational process that cannot be ruled out involves a rapid tautomeric equilibrium prior to the rotation.



If the first step is fast and reversible, the observed rate constant for the rotation is a weighted mean value between those for rotation of the thioamide and for the quinone methide forms. The tautomeric equilibrium must be in favour of the thioamide, since no evidence (UV, IR, and NMR) for the existence of the quinone methide has been obtained. However, this does not preclude the possibility of the existence of a kinetically significant concentration of the quinoid form.

In the ortho-methoxy derivatives and in the α -thio-naphthamides, the thiocarbonyl group is kept out of the plane in the transition state as well, which increases its energy, with a higher barrier as a consequence.

The influence of intermolecular hydrogen bonding alone in the para-hydroxy substituted systems cannot be estimated. The barrier is indeed higher in 16 than 17 but the steric and electronic effects of the tert.-butyl groups in 17 are uncertain.



$$\Delta G^\ddagger = 17.6 \text{ kcal/mol}$$

$$\Delta G^\ddagger = 16.8 \text{ kcal/mol}$$

$$\Delta G^\ddagger = 17.0 \text{ kcal/mol}$$

IV.5 Entropy of activation

In the preceding section the free energies of activation of many compounds have been compared despite the fact that they are measured at very different temperatures. This is of course only possible if the temperature dependence of $\Delta G^\ddagger$, that is the entropy of activation ($\Delta S^\ddagger$), is close to zero. Fortunately, numerous studies on tert. amides and thio-

amides appear to confirm this assumption.⁴³⁻⁵³

In their study on the effect of added phenol on the activation parameters, Siddall et al.³⁴ found that $\Delta S^\ddagger$ is never significantly different from zero although $\Delta G^\ddagger$ increased with phenol concentration. The hypothesis that $\Delta S^\ddagger$ should be more positive because of a loosening of the hydrogen bond in the transition state, thus making this state less ordered than the initial state, then had to be modified. Siddall et al. proposed that the amide-phenol interactions were extended over larger domains than simple amide-phenol pairs and that the shell of surrounding molecules was not disturbed during the time of the rotation.

The model for the rotational process suggested in the preceding section involves weak intramolecular hydrogen bonds in the initial state as well as in the transition state for the ortho-hydroxy substituted thiobenzamides. Consequently, no marked change in intermolecular interactions is to be expected during the time of the rotation.

The entropies of activation for 20 and 24 were determined to be 0.9 ± 1.8 and -2.5 ± 0.5 cal/mol K, respectively. They were measured in different solvents, ODC + fluorobenzene and deuteriochloroform, respectively. These results are in harmony with the expected small change in order in the solution during the rotation.

IV.6 Ultraviolet spectra

The ultraviolet spectra of the thioamides and of some of the corresponding dithioesters are listed in Tables XV and XVI. The spectra were recorded in heptane containing a few percent of methylene chloride.

The ultraviolet spectra of thiones, such as thioamides and dithioesters, contain a characteristic long-wavelength, low-intensity band and a more intense band at shorter wavelengths. It has been shown that the former band is due to the excitation of a non-bonding electron from the sulphur atom to an antibonding π orbital, a $n \rightarrow \pi^*$ transition.⁵⁴⁻⁵⁷ The

classification of this band is based mainly on the effects of substituents and solvent polarity.

Hydrogen bonding usually causes significant perturbations of the electronic transitions of the system, and the most commonly studied effect is the blue shift of the $n \rightarrow \pi^*$ transition,⁵⁸⁻⁶⁰ whereas the shift in the $\pi \rightarrow \pi^*$ transition can be either towards the blue or towards the red.

Comparing the two hydrogen bonded, ortho-hydroxy substituted derivatives 15 and 20 with the two ortho-methoxy analogs 21 and 22, one finds that the $n \rightarrow \pi^*$ band appears at shorter wavelength in the hydrogen bonded species but that the shifts are small, 2 and 8 nm, for 15 and 20, respectively.

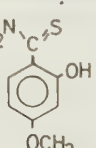
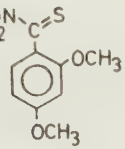
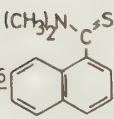
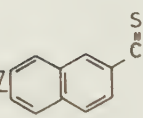
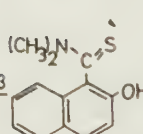
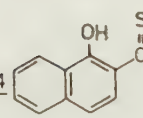
It has been shown⁶¹ that successive N-methylation of thiobenzamide causes hypsochromic shifts of the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ bands due to a departure from coplanarity caused by interference between the methyl groups and the ring hydrogen atoms. According to this observation, the $\pi \rightarrow \pi^*$ bands of 15 and 20 would be expected to appear at longer wavelength than in 21 and 22, respectively, due to the decrease of the angle around the pivot bond upon hydrogen bonding. This is what was observed, but the shifts are small, 9 and 5 nm. However, it was argued in the previous section that it is likely that the ortho-hydroxy derivatives are twisted around both the pivot bond and the thiocarbonyl-nitrogen bond. The deviation from coplanarity around the former bond would make the shift of the $\pi \rightarrow \pi^*$ band less pronounced, and the twist around the carbon-nitrogen bond would probably counteract the bathochromic shift of this band.

It is interesting to make a comparison with the case of the two dithioesters 2 and 3. In 2 there is no steric interaction between the S-methyl group and the ring hydrogen atoms so that the molecule can adopt a planar, strongly hydrogen bonded form. Thus, the $\pi \rightarrow \pi^*$ band of 2 is split into a doublet, the long wavelength part of which is shifted 57 nm towards longer wavelength, while the other remains close to the position of the single band in 3. A similar doubling of the $\pi \rightarrow \pi^*$ band was also found in the ring closed compound N-methyl-1,2,3,4-tetrahydroisoquinoline-1-thione.⁶²

Table XV. Ultraviolet spectra of thioamides.

Compound	Solvent	$\lambda_{\max}$ nm	$\log \epsilon$	$\lambda_{\max}$ nm	$\log \epsilon$	$\lambda_{\max}$ nm	$\log \epsilon$
$(\text{CH}_3)_2\text{N}-\text{C}(=\text{S})-\text{C}_6\text{H}_5$ 	a heptane	395	2.50	284	3.93	250	3.95
CH_3 $\text{S}=\text{N}-\text{C}_6\text{H}_4$ 	b heptane	425	2.09	323	3.81	299	3.71
$(\text{CH}_3)_2\text{N}-\text{C}(=\text{S})-\text{C}_6\text{H}_4\text{OH}$ <u>15</u>	heptane + 10% CH_2Cl_2 0.5% CH_2Cl_2	377	2.90	290	4.01	242	3.91
$(\text{CH}_3)_2\text{N}-\text{C}(=\text{S})-\text{C}_6\text{H}_4\text{OCH}_3$ <u>22</u>	heptane + 10% CH_2Cl_2 0.5% CH_2Cl_2	379	2.48	281	4.03	245	3.93
$(\text{CH}_3)_2\text{N}-\text{C}(=\text{S})-\text{C}_6\text{H}_4\text{OCH}_3$ <u>28</u>	heptane + 10% CH_2Cl_2 0.5% CH_2Cl_2	389	2.73	276	4.16	253	4.18
$(\text{CH}_3)_2\text{N}-\text{C}(=\text{S})-\text{C}_6\text{H}_4\text{OH}$ <u>16</u>	heptane + 10% CH_2Cl_2 0.5% CH_2Cl_2	383	2.75	276	4.13	259	4.06

Table XV. cont.

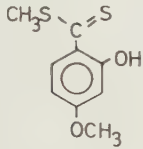
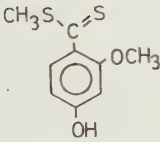
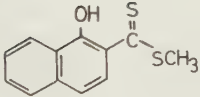
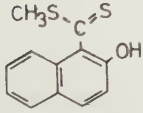
Compound	Solvent	$\lambda_{\max}$ nm	$\log \epsilon$	$\lambda_{\max}$ nm	$\log \epsilon$	$\lambda_{\max}$ nm	$\log \epsilon$
20 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	370	3.16	288	4.04	279	4.04
21 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	378	2.75	283	4.11	255	4.09
26 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	379	2.58	304 ^c	3.89	275	4.13
27 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	384	2.84	295 ^c	4.03	285.5	4.13
23 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	382	3.07	334	3.56	285	4.06
24 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	373	3.46	346	3.49	289 ^c	4.13
						277.5	4.21

a Ref. 61.

b Ref. 62.

c Shoulder.

Table XVI. Ultraviolet spectra of dithioesters.

Compound	Solvent	$\lambda_{\max}$ nm	$\log \epsilon$	$\lambda_{\max}$ nm	$\log \epsilon$	$\lambda_{\max}$ nm	$\log \epsilon$
<u>2</u> 	heptane + 10% CH ₂ Cl ₂ 0.5 % CH ₂ Cl ₂	450 ^a	2.53	381	4.26	324	4.21
<u>3</u> 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	486	2.30			325	4.12
<u>6</u> 	heptane + 0.5% CH ₂ Cl ₂	439	4.04	422	4.06	330	4.37
<u>4</u> 	heptane + 10% CH ₂ Cl ₂ 0.5% CH ₂ Cl ₂	478 ^a	2.46	401	3.08	328	3.85

^a Shoulder.

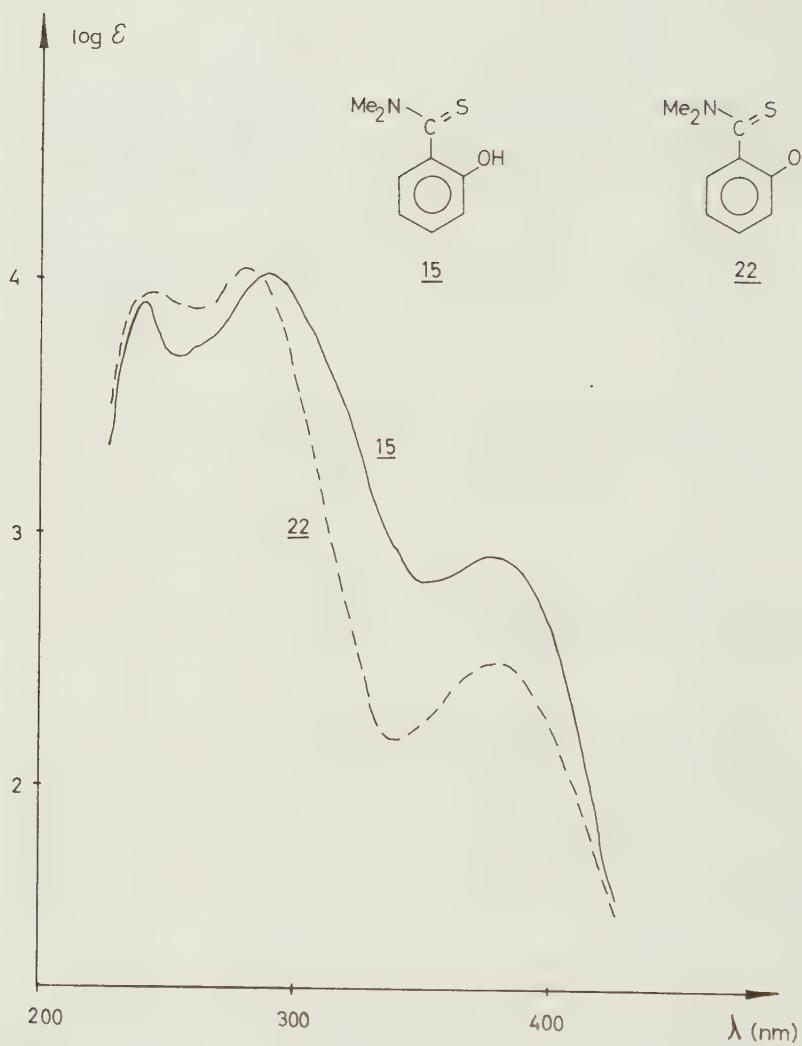


Fig. 6a UV spectra of 15 and 22 in heptane.

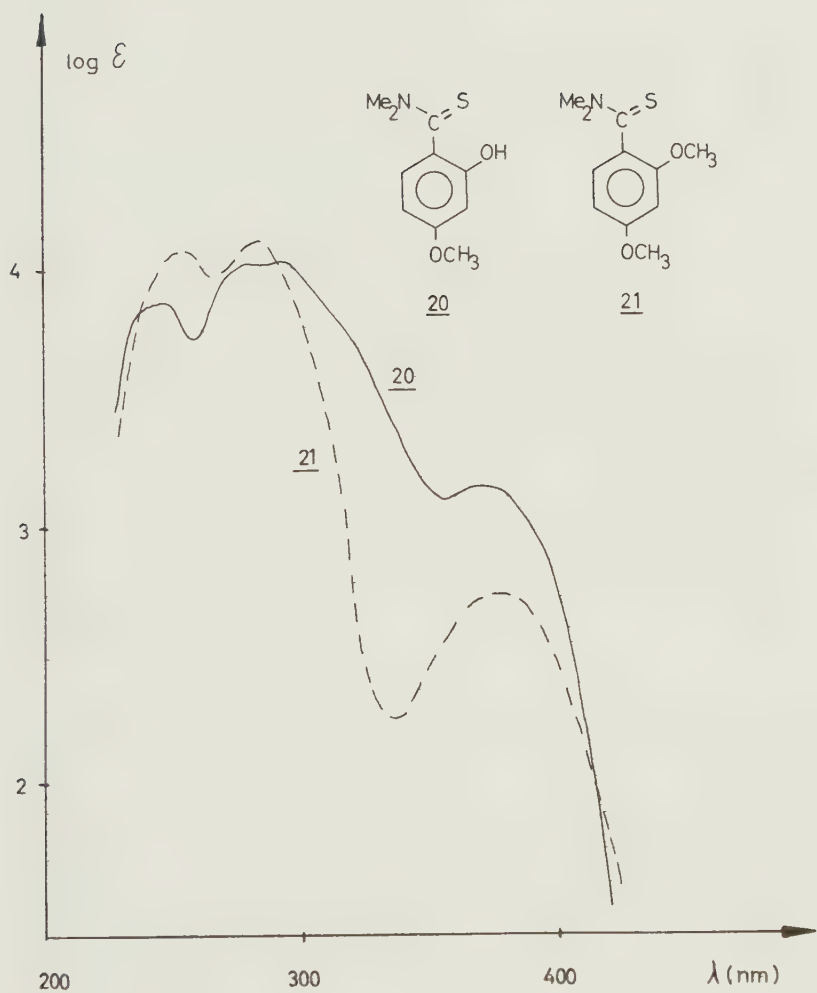


Fig. 6b UV spectra of 20 and 21 in heptane.

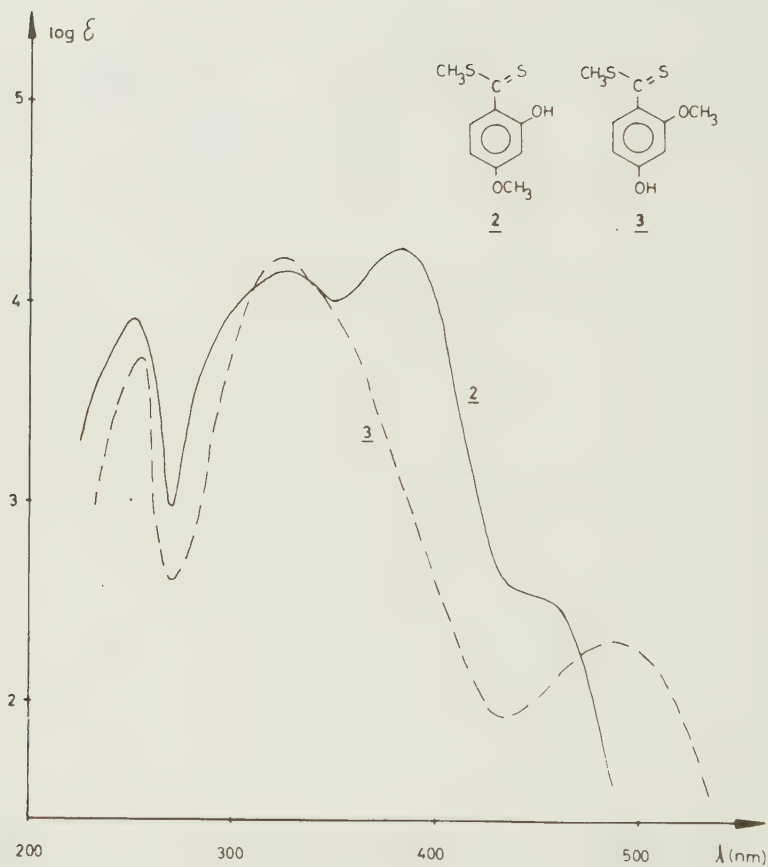


Fig. 6c UV spectra of 2 and 3 in heptane.

Furthermore, the $n \rightarrow \pi^*$ band of 2 appears at 36 nm towards shorter wavelength than in 3, in agreement with the normal behaviour of $n \rightarrow \pi^*$ bands upon hydrogen bonding (Fig. 6).

Sandström⁶⁰ observed an increase in oscillator strength on going from thiobenzamide to N,N-dimethylthiobenzamide, and ascribed this to the increasing departure from coplanarity between the thioamide group and the benzene ring, which causes an increased mixing of the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. Large oscillator strengths were found for the thioamides studied in this investigation as well, but the effect was much more pronounced for the ortho-hydroxy derivatives (Table XVII). This enhanced effect can be understood in view of a departure from coplanarity in the thioamide group. The lone pair orbital on the sulphur atom can now overlap with the p orbital on the nitrogen atom since these orbitals are no longer orthogonal.

The oscillator strengths have been calculated with the aid of the formula $f = 4.31 \times 10^{-9} \times \epsilon_{\max} \times 2 (\nu_{\max} - \nu_{0.5})$, where $\nu_{0.5}$ is the wave number on the low frequency side of the band at which the extinction has decrease to half of the maximum value.

Table XVII. Oscillator strengths for the $n \rightarrow \pi^*$ transition in some thiobenzamides.

Compound	Oscillator strength
Thiobenzamide	0.0035
N,N-Dimethylthiobenzamide	0.0046
<u>15</u>	0.011
<u>20</u>	0.021
<u>24</u>	0.045

V. QUINONE METHIDES

V.1 Introduction

Rotation about carbon-carbon double bonds usually involves high energy barriers. For example, the barrier for cis-trans isomerism in 1,2-dideuterioethylene is as high as 60 kcal/mol.⁶³ There are a number of ways in which the energy barrier may be significantly lowered, including stabilization of the diradical or dipolar transition states, or destabilization of the planar ground state, usually by non-bonded interactions. This field has been reviewed by Binsch,¹ Sutherland² and Kessler.³ Most of the examples which have been reported involve stabilization of a dipolar transition state. Substitution of one carbon atom of the double bond with electron-donating groups, and of the other with electron-withdrawing groups diminishes the double bond character.



The negative part of the transition state may be stabilized by CO_2R , COR, CN, NO_2 and $\text{p-NO}_2\text{C}_6\text{H}_4$ substituents, and the positive part by substituents such as NR_2 , OR and SR.

This investigation was intended to be a study of systems in which the electron-attracting group, by accepting one electron pair, may assume aromatic character. Kende et al.⁶⁴ have studied the rotational barrier in the substituted calicene 51.



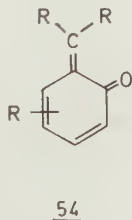
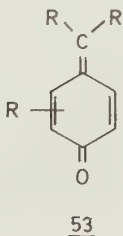
51

52

Incorporation of the double bond π electrons into the cyclopentadienyl system results in the creation of two aromatic systems, thus giving a transition state of low energy. The existence of a dipolar transition state is supported by the solvent effect, as a polar solvent may stabilize the transition state better than a non-polar solvent. Kende *et al.*⁶⁴ found an activation energy ($\Delta G^\ddagger$) of 19.2 kcal/mol in ODC and 18.0 kcal/mol in DMF.

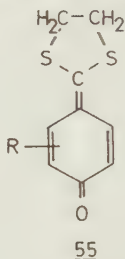
The C(1)=C(6) barrier in 6-dimethylaminofulvene (52) has been found to be 22.1 kcal/mol.^{65,66} This compound also shows a moderately high barrier to rotation about the C(6)-N bond, 13.5 kcal/mol.^{65,66} The effect of solvent changes upon the C(1)=C(6) rotational barrier is likewise in accordance with a dipolar transition state. The low activation energies for the C=C double bond rotation process demonstrates the ease of polarization in these compounds and does not necessarily imply a high degree of aromaticity in the initial state. SCF MO treatment predicts bond orders and bond lengths close to those for pure double bonds, as well as resonance energies that are small for unsubstituted fulvene and calicene.⁶⁷ Coupling constant measurements, dipole moment data, the C(1)=C(6) rotational barrier and delocalization energy, however, prompted Downing, Ollis and Sutherland⁶⁵ to suggest that 6-dimethylaminofulvene should be described as an aromatic compound.

Another system which can assume aromatic character by polarization is the quinone methide system, *e.g.* 53 or 54.



Simple quinone methides, unsubstituted or alkyl substituted on the exocyclic carbon, have not been isolated, and attempts to prepare them have usually resulted in dimers or trimers.^{68,69} The monomer has been spectroscopically detected in solution.⁷⁰ The participation of quinone methides as reactive intermediates in the biosynthesis of lignin has been discussed.⁷¹⁻⁷³

Quinone methides with electron-donating substituents on the exocyclic carbon are usually somewhat more stable. Their reactivity toward nucleophiles and electrophiles is high, but they show no tendency to polymerize. Gompper *et al.*⁴ have isolated some ω,ω -bis(alkylthio)quinone methides of the type 55

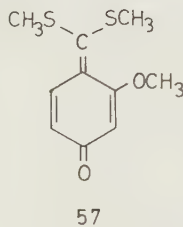
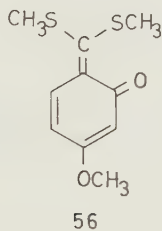


which are of higher stability than the open chain ω,ω -bis-(methylthio)quinone methides, and they have discussed the contribution of the dipolar resonance structures of 53 and 54 to the initial state as reflected in IR and UV spectra and dipole moments. From these results they estimated the contribution of the dipolar structures to be 10-20 %.

In order to acquire further understanding of the importance of dipolar resonance contributors and of the π -electron delocalization energy of these systems, it was intended to investigate the barrier to rotation around the exocyclic C-C double bond in quinone methides with two methylthio groups on the methide carbon atom. It was also the purpose to study the carbon-nitrogen torsional barrier in quinone methides substituted with one methylthio group and one dimethylamino group.

V.2 Results and discussion of the spectra of the individual compounds

5-Methoxy-1,2-benzoquinone-bis(methylthio)methide-(2)
(56) and 3-methoxy-1,4-benzoquinone-bis(methylthio)methide-(4)
(57)

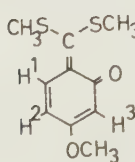
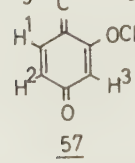


The NMR parameters of 5-methoxy-1,2-benzoquinone-bis(methylthio)methide-(2) (56) and of 3-methoxy-1,4-benzoquinone-bis(methylthio)methide-(4) (57) are shown in Table XVIII. In both compounds the methylthio groups gave rise to a singlet at probe temperature, but the signal of 56 was somewhat broadened. When 56 was cooled (in CS_2) the S-methyl signal was further broadened, and at 22.2°C it split into a symmetrical doublet, the two signals of which were separated by 6.3 Hz at -24°C . This was interpreted as being due to slow rotation around the exocyclic carbon-carbon double bond with a barrier ($\Delta G^\ddagger$) of 15.7 kcal/mol.

For compound 57 no splitting of the S-methyl signal was observed down to -120°C in any of the solvents CS_2 , CHCl_2F or $\text{CH}_2\text{Cl}_2 + \text{C}_6\text{H}_5\text{F}$ (1:1). This may be explained by a rapid rotation on the NMR time scale around the $\text{C}=\text{C}$ bond even at -120°C , which would imply a barrier below 8.5 kcal/mol with an assumed $\delta\nu$ of 2 Hz or higher. An alternative interpretation would be an accidental chemical shift equivalence of the two S-methyl groups at slow exchange.

The explanation in terms of a low rotational barrier is somewhat unexpected in view of the general picture of the stability of ortho-quinoid and para-quinoid systems, according

Table XVIII. NMR parameters for 56 and 57.

Chemical shifts ^a		Coupling constants (Hz)	
 <u>56</u>	CH ₃ S	2.52	
	(broad singlet)		
	CH ₃ O	3.73	
	H ₁	7.42	$J_{1,2} = 9.5$
	H ₂	5.93	$J_{2,3} = 2.5$
	H ₃	5.53	$J_{1,3} \approx 0$
 <u>57</u>	CH ₃ S	2.53	
	CH ₃ O	3.79	
	H ₁	7.73	$J_{1,2} = 10.1$
	H ₂	6.02	$J_{2,3} = 1.8$
	H ₃	5.65	$J_{1,3} \approx 0$

^a δ from TMS at room temperature. Solvent: CS₂.

to which the latter system is more stable. However, this argument is only valid under the assumption that the main part of the barrier difference between 56 and 57 can be related to the energy of the initial state.

Since the main part of the energy barrier to rotation in these systems can be attributed to the difference in π -stabilization between the initial and transition states, the barrier has been calculated by the Pariser-Parr-Pople (PPP) method. (The application of the PPP-method to the calculation of rotational barriers used in this work is presented in Chapter VI.) Idealized geometries were assumed for the ring. The bond lengths in the bis-methylthio methylene group were determined by an iterative process described in section VI.7. The values are reproduced in Table XIX.

Table XIX. Bond lengths and bond angles used in the PPP calculation.

	Bond length (Å)	
	Initial state	Transition state
S-C	1.68, 1.69	1.64
C-C (exocyclic)	1.40	1.47
C-C (ring)	1.40	1.40
C=O	1.23	1.23
C-O	1.33	1.33
	Angle (degrees) ^a	
S-C-S	116	
S-C-C	122	
C-C-C	120	
C-C-O	120	

^a In the transition state the bis-methylthio methylene group was twisted 90° out of the ring plane.

The π -electron energies (E_{π}) and core repulsion energies (E_{core}) obtained by the calculations are summarized in Table XX, and the bond orders and charge densities in Figs. 7 and 8.

The rotational barriers calculated by the PPP-method are 19.2 kcal/mol for 56 and 22.7 kcal/mol for 57. These values have been calculated according to equation (21) on page 101

The calculated value for 56 satisfactorily reproduces the experimental result, even if the possible sources of errors in comparisons between experimental and calculated barriers are considered. (These errors are discussed in section VI.10.) According to the calculated value for 57 this compound should have a 3.5 kcal/mol higher barrier than 56

Table XX. E_{π} and E_{core} for 56 and 57 from PPP calculations (eV).

<u>56</u>			
	Initial state	Transition state	ΔE
E_{π}	-505.5554	-504.0693	1.4861
E_{core}	295.6190	294.9636	-0.6554
E_{tot}	-209.9364	-209.1057	0.8307

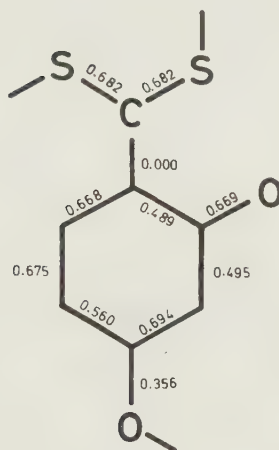
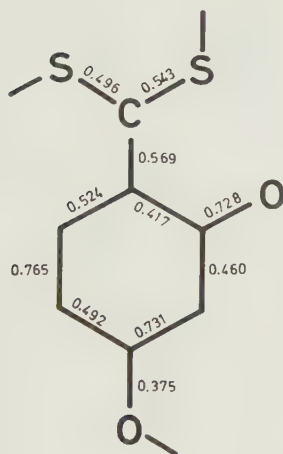
<u>57</u>			
	Initial state	Transition state	ΔE
E_{π}	-512.2795	-509.6829	2.5966
E_{core}	302.8126	301.1991	-1.6135
E_{tot}	-209.4669	-208.4838	0.9831

and it is interesting to note that this result is obtained, in spite of the 10.8 kcal/mol lower initial state energy of 56 compared to 57 (Fig. 9).

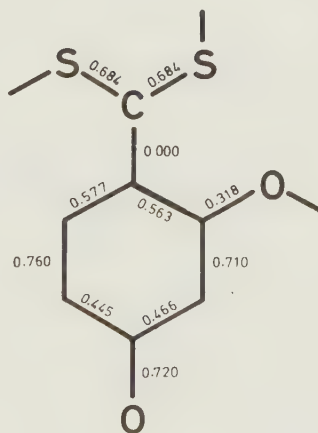
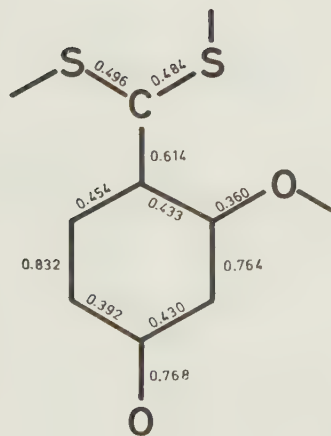
It has been pointed out that a relationship between vicinal coupling constants and bond orders has a theoretical justification.⁷⁴ For this reason, a comparison of the coupling constants for the ring protons of 56 and 57 can lead to a qualitative estimate of π -electron delocalization. It is also interesting to include the ortho-coupling constants of 2 and 3 in the comparison.

Initial state

Transition state



56

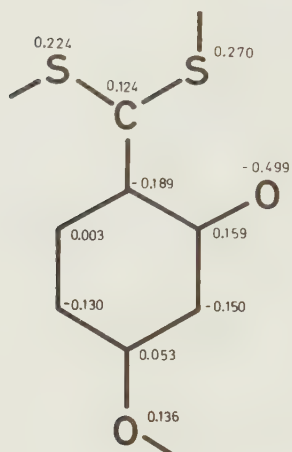


57

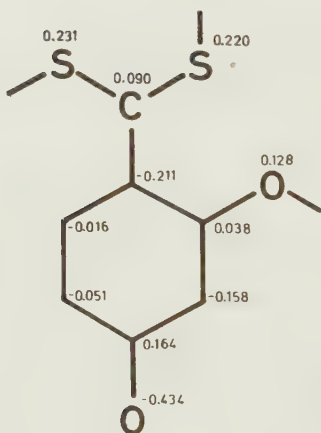
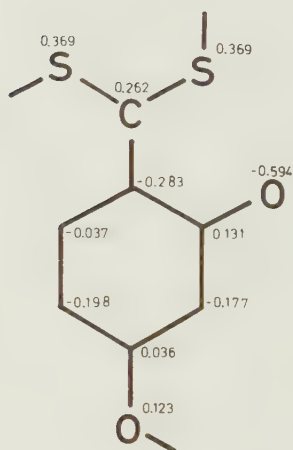
Fig. 7 Bond orders from PPP calculations.

Initial state

Transition state



56



57

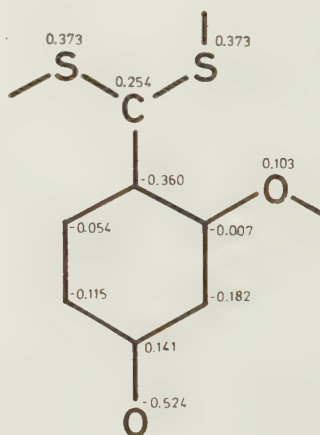


Fig. 8 Charge densities from PPP calculations.

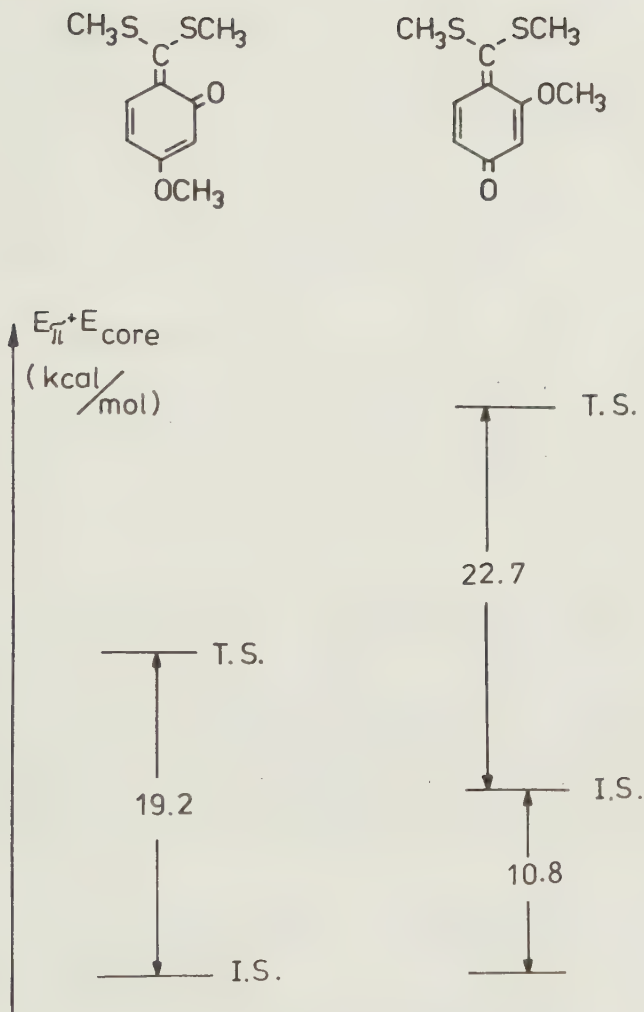
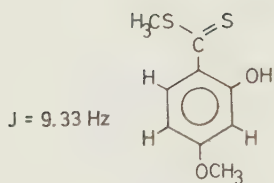
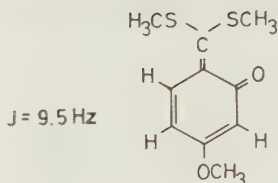


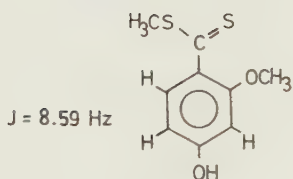
Fig. 9 Initial state and transition state energy levels for the rotational process obtained from the PPP calculations.



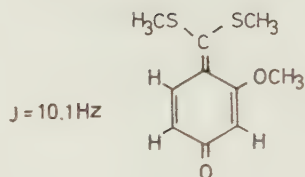
2



56

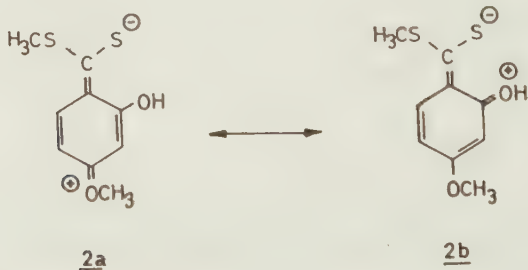


3



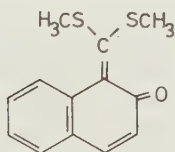
57

The larger coupling constant of 2 compared to that of 3 is consistent with a more pronounced interaction between the ring and the dithioester group in 2 than in 3. For 2 it was proposed that the dithioester group and the ring were coplanar due to hydrogen bonding, making resonance structures such as 2a and 2b more important, whereas for 3 this conjugation is partly inhibited due to the sterically induced twist of the dithioester group.

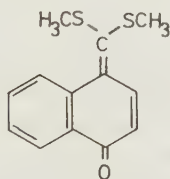


Both of the resonance structures indicate a higher bond order of the bond in question. The corresponding coupling constants for 56 and 57 are 9.5 Hz and 10.1 Hz, suggesting a higher degree of π -electron delocalization of the C-C bond in 56. These data are in good agreement with the calculated bond orders, which are 0.765 for 56 and 0.832 for 57.

1,2-Naphthoquinone-bis(methylthio)methide-(1) (58) and 1,4-naphthoquinone-bis(methylthio)methide-(4) (59).



58



59

The NMR spectrum of 58 in carbon disulphide at room temperature consists of one sharp singlet for the S-methyl protons ($\delta = 2.30$, 6 protons), a multiplet for five of the ring protons ($\delta = 6.88-7.33$, 5 protons), and one part of an AB quartet ($\delta = 6.46$, $J = 9.8$ Hz, 1 proton) for the protons in the 3- or 4-position, probably the 3-proton.

Compound 59 exhibits a spectrum very similar to that of 58. The S-methyl protons again give a singlet ($\delta = 2.47$, 6 protons) and one part of an AB quartet ($\delta = 6.37$, $J = 10.0$ Hz, 1 proton) is isolated from the multiplet ($\delta = 7.33-8.75$, 5 protons) containing the other part of the AB quartet and the other ring protons. The results from the barrier measurements are summarized in Table XXI.

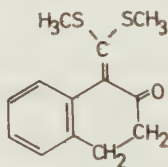
The $\Delta G^\ddagger$ values for 58 and 59 are unexpectedly low from electronic point of view, since the energy gain of creating a benzenoid system can be expected to be larger than that of forming a naphthenoid structure from a precursor already containing one aromatic ring. For example, considering the resonance energies of benzene (36.0 kcal/mol) and naphthalene (61.0 kcal/mol)⁷⁵ the difference in energy gain is 11.0

Table XXI. Results of barrier measurements of 58 and 59.

Compound	Solvent	$\delta\nu$ (Hz)	T_c (K)	$\Delta G^\ddagger$ (kcal/mol)
<u>58</u>	CS_2	29.4	160 $\pm$ 4	7.8 $\pm$ 0.2
<u>59</u>	$CS_2 + 10\% CH_2Cl_2$	42.0	170 $\pm$ 4	8.2 $\pm$ 0.2

kcal/mol. The observed low activation energies for 58 and 59 probably have their explanation in a destabilization of the initial state by a steric interaction between the peri-hydrogen and the neighbouring methylthio group.

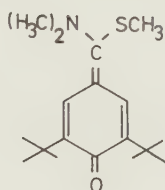
On the other hand it seem obvious that the transition state of 58 (and consequently those of 56, 57 and 59) is considerably stabilized by resonance by comparison of the rotational barriers in 58 and 60.



60

The activation energy ($\Delta G^\ddagger$) for the rotation of 60 is 23.3 kcal/mol⁷⁶ which is 15.5 kcal higher than the barrier in 58. The effects of steric interactions in these compounds are very similar, so that the main part of the difference in barrier of 15.5 kcal comes from a π -electron stabilization of the transition state of 58.

2,6-Di-tert.-butyl-1,4-benzoquinone-[dimethylamino-methylthio-methide-(4)] (61).



61

The NMR spectrum of this compound at room temperature shows 4 signals, all sharp singlets. The chemical shifts are given in Table XXII.

Table XXII. Chemical shifts for 61 in CS₂

δ (ppm from TMS)	
(CH ₃) ₃ C	1.25
CH ₃ S	2.34
(CH ₃)N	3.33
ring	7.04

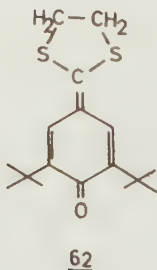
Below -60°C all four singlets broaden and at -90°C and down to -120°C the spectrum contains four extremely broadened signals. The same behaviour was observed in CHCl₂F as in CS₂, and did not arise from crystallization or high viscosity of the solution. The dimethylamino signal showed no tendency to broaden more than the other signals. These results suggest an unexpectedly low rotational barrier around the C-N bond. Steric interference between the dimethylamino group and the tert.-butyl groups is probably not an explanation for the low barrier, since examination of a Dreiding model of 61 indicates that the distance between the groups is too great. The same

steric interaction between the dimethylamino group and the ring hydrogen as discussed in section IV.4 for the thiobenzamide is a more probable explanation. This effect may be accentuated by buttressing of the ortho-hydrogen by the tert.-butyl groups.

V.3 Conclusions

The low barriers to rotation around the exocyclic carbon-carbon double bond in bis(methylthio)quinone methides demonstrate the ease of polarization of these compounds. The barrier alone, however, is not well suited to estimate the degree of π -electron delocalization in these molecules since it measures the energy difference between two states. More information may be obtained by comparison with an appropriate reference system. Thus, a comparison of the barriers in 58 and 60 indicates that the transition state for the rotational process in 58 is resonance stabilized to a high degree. The ring systems may assume aromatic character, as illustrated in Fig. 10 for compound 56.

An indication of the importance of charge separation in the initial state is given by the relatively high dipole moments of these compounds. Thus, compound 62 has a dipole moment of 6.36 D,⁴ which indicates that the dipolar character is about 15-17 %.



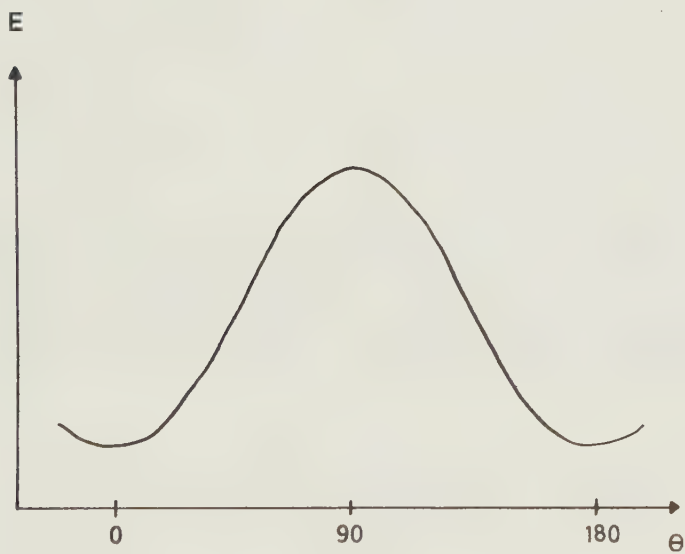
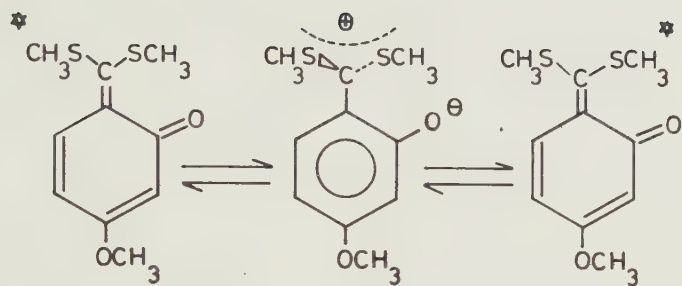
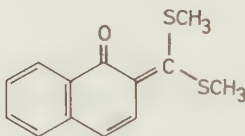


Fig. 10 Assumed potential curve for the rotational barriers.

The PPP calculations suggest the ortho-quinone methide structure to be more stable than the para-quinone methide structure. When the methoxy groups are excluded in the calculations this relation is maintained. Furthermore, an examination of the bond orders lead to the proposal that the π -electrons are more delocalized in the ortho-quinone methide system than in the para-quinoid analogue. This is also confirmed by the coupling constants. The reason for this may be the greater electrostatic work necessary to separate charge over a greater distance in the para-quinoid systems, the negative charge being localized mainly on the carbonyl oxygen atoms.

The calculations also predict the rotational barrier in 57 to be higher than that in 56. The difference in steric strain, not included in the calculations, can not explain a barrier-lowering of ca. 10 kcal/mol needed to reach a barrier of 8.5 kcal/mol. Thus, if the calculations are reliable, an accidentally small chemical shift between the S-methyl groups is the most reasonable explanation for the experimental results.

The barrier lowering effect of benzene annelation (compounds 58 and 59) probably results from the steric interaction between the peri-hydrogen and the adjacent methylthio group, and not from electronic effects. Attempts to prepare compound 63 in which this steric interaction is removed were unsuccessful.



63

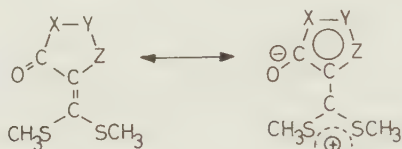
Rotational barriers around the C(6)-N bond in the fulvene series are lowered by benzene annelation.^{65,77} It has been observed that polarized ethylenes with high C=C barriers generally have the lowest C-N barriers and vice versa.^{76,78}

This line of argument applied to the compounds under consideration, would mean that C=C barriers are raised upon benzene annelation.

VI. AZOLINONES

VI.1 Introduction

In the preceding chapter rotational barriers around carbon-carbon double bonds were studied in polarized ethylenes, one of the carbon atoms of which was built into a carbocyclic ring capable of forming an aromatic 6- π -electron system. This investigation has been extended to five-membered heterocyclic analogues containing two heteroatoms in the ring.



The tendency of the different systems to become aromatic may be expected to affect the barrier to rotation around the exocyclic double bond. The barriers have been calculated by SCF-MO methods and the results from the calculations have been compared with the experimental observations. Ultraviolet spectra of the compounds have also been compared with the transition energies obtained from the calculations.

The compounds studied are summarized in Fig. 11.

VI.2 Results of barrier measurements

Examination of the NMR spectra of compounds 29-40 at the coalescence temperature provided a set of ΔG_{TC}^* values for the barriers to internal rotation around the exocyclic carbon-carbon double bond. The measurements were carried out in 0.5-0.7 M ortho-dichlorobenzene solutions. Compound 29 was also studied by complete lineshape analysis in the same solvent. The ΔG^* value at the coalescence temperature obtained from this study was, however, 1.5 kcal/mol lower than the value obtained by the approximate method. This discrepancy

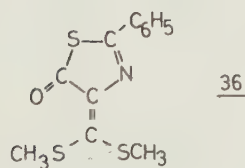
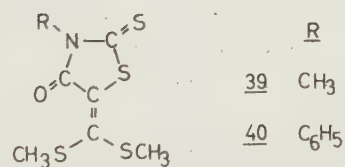
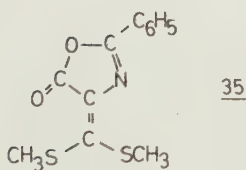
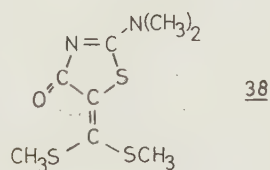
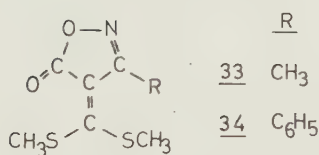
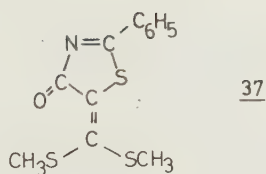
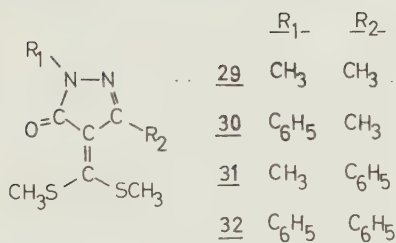


Fig. 11 The structures of the molecules in this investigation.

is much larger than usual, and prompted further investigations.

VI.3 Concentration dependence of the rotational barriers

The effect of concentration on $\Delta G_{TC}^{\ddagger}$ was studied for compounds 29, 30, 31, 33 and 34 in ODC. The results are shown in Fig. 12. $\Delta G^{\ddagger}$ values were determined at the coalescence temperature, which varies over a range of 140° for the different compounds. $\Delta G^{\ddagger}$ for 29 increases ca. 7 kcal/mol when the concentration of the solute is decreased from 1 M to 0.1 M. For 31 the corresponding increase is ca. 3.5 kcal/mol. Almost all of this drastic change falls within a narrow concentration interval, while at higher concentrations the barrier is practically independent of concentration and, for 29, the curve is also flattened out at lower concentrations (< 0.2 M). The concentration dependence was also studied in benzonitrile, and the results are shown in Fig. 13.

Also in this solvent 29 and 31 display a strong concentration dependence of the barrier. The curve of 29 in benzonitrile, however, differs substantially from the curve in ODC. Thus the low concentration values in benzonitrile fall about 2 kcal/mol below the corresponding values in ODC. Furthermore, the steep part of the curve is less pronounced in benzonitrile and a considerable concentration dependence was found at higher concentrations. For 31 a sigmoidal dependence of $\Delta G^{\ddagger}$ on concentration similar to that found for 29 in ODC was observed.

VI.4 Catalytic effects of acid and base and of impurities

In order to determine whether the observed behavior was a true effect of concentration or if it was a catalytic effect of small amounts of impurities in the solvents or in the substances, the investigation was continued by checking the purity of the samples and by an examination of the influence of acids and bases on the barrier.

A thin layer chromatographic study (silica, chloroform-

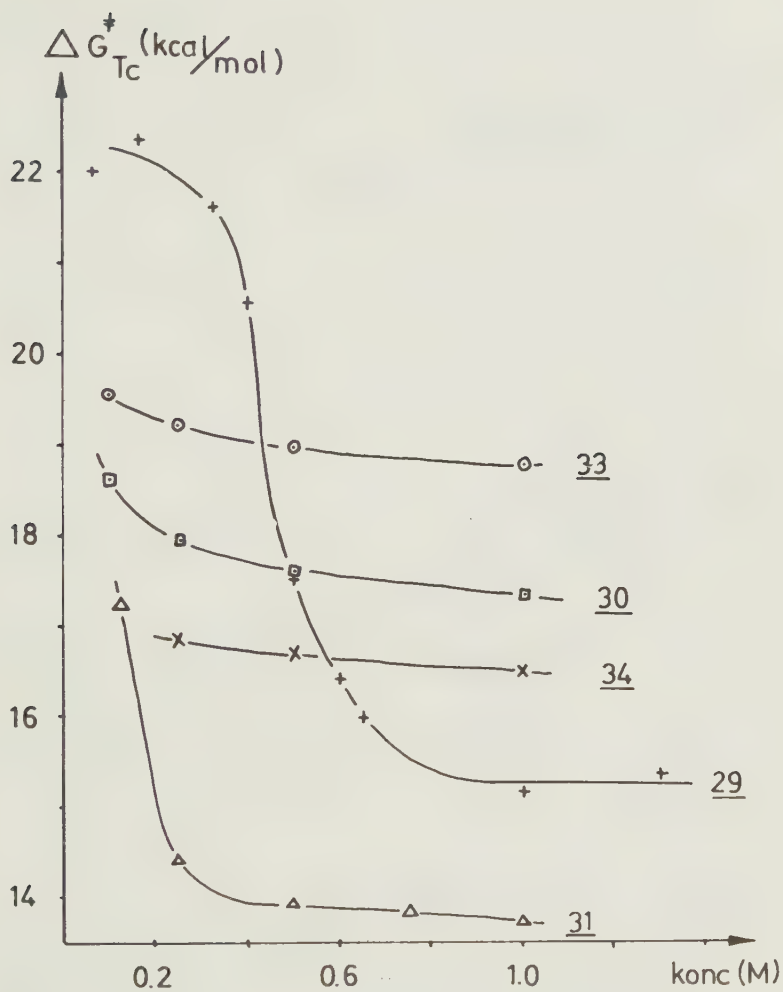


Fig. 12 Concentration dependence of $\Delta G^{\ddagger}$ in ODC.

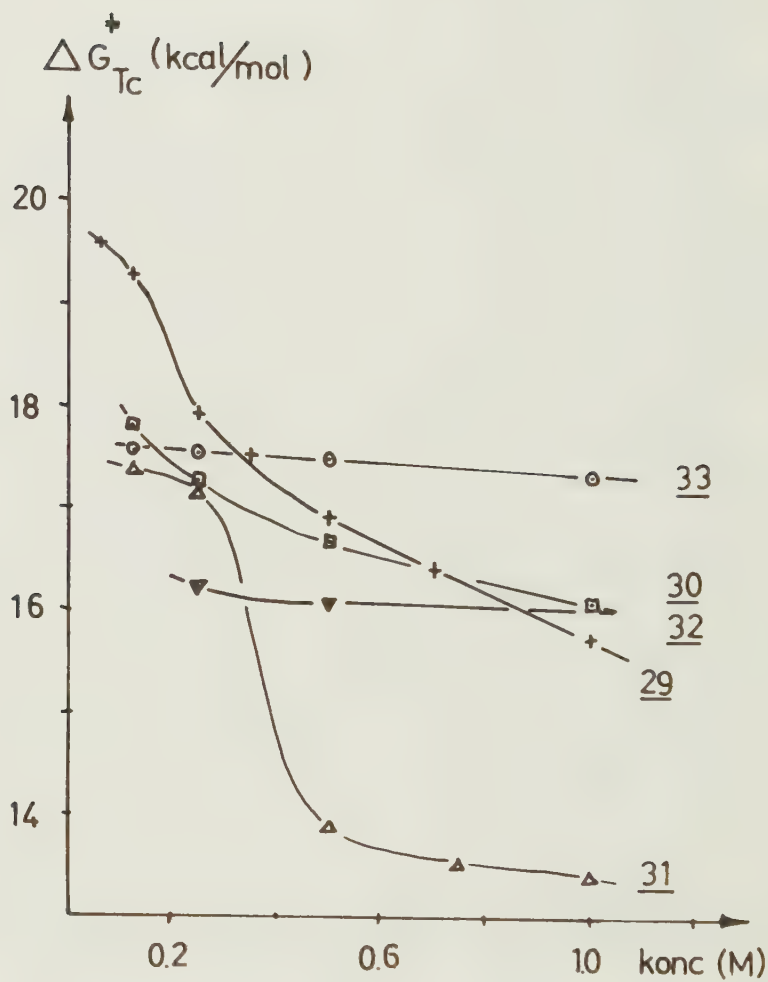


Fig. 13 Concentration dependence of $\Delta G^\ddagger$ in benzonitrile.

-ethylmethylketone) of 29 showed that in addition to the orange spot from 29 ($R_f = 0.56$), a small spot ($R_f = 0.19$) could be observed in UV light. This impurity was isolated from 3.0 g material by chromatography through a silica column, from which 29 was eluted with ether and the impurity with acetone-methanol (4:1). 20 mg of pale yellow, high melting ($> 260^\circ$) crystals were isolated. The substance was practically insoluble in most organic solvents but was slightly soluble in water. It was not possible to determine its structure by spectroscopic methods. The impurity was apparently formed by decomposition of 29 since the barrier of a sample which had been kept under dry conditions for a year was lower than that of the same sample measured immediately after its preparation. Freshly prepared 29 did not contain this impurity.

Barrier measurements for pure 29 at different concentrations in ODC and benzonitrile, and for pure 29 with added trifluoroacetic acid, and with the crystals isolated in the chromatographic experiment, are summarized in Table XXIII.

Addition of one drop 2,4-lutidine* to samples g and h caused an increase of the barrier to ca. 21 kcal/mol. An analogous enhancement of the barrier also occurred on addition of 2,4-lutidine to the original contaminated 29.

Thin layer chromatography of 30 and 31 indicates the presence of no impurity. However, a barrier increasing effect of 2,4-lutidine was observed. The results are given in Table XXIV. The results suggest that 30 and 31 were contaminated by an acidic impurity.

Addition of 2,4-lutidine to pure 29 and to 32, 33 and 34 did not raise the barriers more than 0.2 kcal/mol. The experimental barriers of these compounds can thus be considered to be unaffected by acidic catalysts. Results of the barrier measurements of all the studied compounds are summarized in Table XXV. 30 and 31 were treated with one drop 2,4-lutidine, corresponding to a concentration of about 0.1 M.

* Lutidine was used since pyridine was found to react with the azolinones at elevated temperatures.

Table XXIII. Effect of solvent, concentration, acid and the isolated impurity on the rotational barrier in purified 29.

Sample	Solvent	[<u>29</u>] (M)	$\delta\nu$ (Hz)	T_c (K)	ΔG^* (kcal/mol)
a	ODC	1.0	8.5	403.0	21.5
b	ODC	0.50	8.5	404.3	21.5
c	ODC	0.25	8.6	405.8	21.6
d	C_6H_5CN	1.0	9.8	371.3	19.6
e	C_6H_5CN	0.50	8.5	373.4	19.8
f	C_6H_5CN	0.25	8.2	373.9	19.9
g + 0.01 M CF_3COOH	ODC	1.0	8.2	256.0	13.4
h + 2% w/w impurity	ODC	1.0	8.1	256.7	13.5

Table XXIV. Effect of 2,4-lutidine on the barrier of 30 and 31 (solvent: ODC).

Sample	Conc. (M)	$\delta\nu$ (Hz)	T_c (K)	ΔG^* (kcal/mol)
<u>30</u>	1.0	10.3	330.9	17.4
<u>30</u> + 1 dr. 2,4-lutidine	1.0	10.9	358.3	18.8
<u>31</u>	1.0	57.4	279.3	13.6
<u>31</u> + 1 dr. 2,4-lutidine	1.0	52.8	365.6	18.1

Table XXV. Results of barrier measurements using formula (10)
(solvent: ODC).

Compound	Conc. (M)	$\delta\nu^b$ (Hz)	T _c (K)	$\Delta G^\ddagger$ (kcal/mol)
<u>29</u>	1.0	8.5	403.0	21.5
<u>30</u> ^a	1.0	10.9	358.3	18.8
<u>31</u> ^a	1.0	52.8	365.6	18.1
<u>32</u>	1.0	52.0	328.1	16.2
<u>33</u>	1.0	4.7	346.8	18.8
<u>34</u>	1.0	43.0	331.1	16.5
<u>35</u>	0.6		≥ 470	>25
<u>36</u>	0.6		≥ 470	>25
<u>37</u>	0.6		≥ 470	>25
<u>38</u>	0.6		≥ 470	>25
<u>39</u>	0.6		≥ 470	>25
<u>40</u>	0.6		≥ 470	>25

^a One drop of 2,4-lutidine was added to the sample.

^b 60 MHz.

The uncatalyzed barriers may be 0.1 to 0.5 kcal/mol higher, in analogy with what was found for 29.

The results of the complete lineshape analysis of 29 containing ca. 1 % acidic impurity is presented in Table XXVI.

VI.5 Discussion of the barriers

Sandström and Wennerbeck⁶ determined rotational barriers in 1,1-bis(alkylthio)ethylenes with electron-withdrawing groups in the 2-position in the range 18 to more than 25

Table XXVI. Results from the complete lineshape treatment of 29 containing ca. 1 % acidic impurity (solvent: ODC).

T (K)	$\delta\nu$ (Hz)	$(T_2)_1$	$(T_2)_2$ (sec) ^a	τ (sec)	$\Delta G^\ddagger$ (kcal/mol)
328.2	8.75	0.817	0.777	0.163	18.1
331.4	8.64	0.817	0.777	0.145	18.2
335.0	8.49	0.861	0.817	0.121	18.3
338.0	8.43	0.838	0.796	0.113	18.4
440.9	8.43	0.965	0.910	0.097	18.4
344.2	8.60	0.777	0.741	0.081	18.5
348.3	8.27	0.965	0.910	0.070	18.7
352.1	8.23	1.062	0.995	0.060	18.8
355.9	8.19	0.965	0.910	0.052	18.9
359.6	8.15	0.885	0.838	0.043	18.9
362.7	8.13	0.885	0.838	0.038	19.0
366.4	8.11	0.910	0.861	0.032	19.1
369.6	8.10	0.910	0.861	0.028	19.2
372.7	8.09	0.995	0.937	0.024	19.2

^a $\Delta\nu_{1/2}$ was found to be 0.02 Hz greater for one of the S-methyl signals.

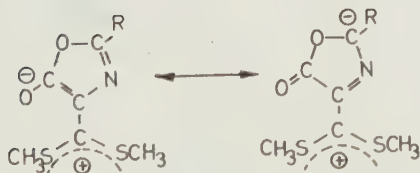
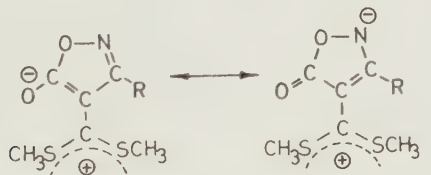
$$\Delta H^\ddagger = 9.8 \pm 0.2 \text{ kcal/mol}$$

$$\Delta S^\ddagger = -25.5 \pm 0.5 \text{ cal/mol K}$$

The errors are standard deviations from the least-squares plot.

kcal/mol ($\Delta G_{TC}^{\ddagger}$). The pyrazolinone and isoxazolinone systems studied in this work have barriers between 16 and 22 kcal/mol, depending upon the substituents, whereas the oxazolinone and thiazolinone systems have barriers that are higher than 25 kcal/mol. Thus it can be concluded that the barriers in the present work are of about the same magnitude as those found by Sandström and Wennerbeck⁶ and that the pyrazolinone and isoxazolinone systems are as effective as the most powerful combination of electron-attracting groups (*e.g.* COC_6H_5 , CN , COOC_2H_5 and COCH_3) in stabilizing a negative charge.

The barriers in the heterocyclic ring systems with the two heteroatoms adjacent to each other in the ring are lower than the barriers in systems with the heteroatoms in a 1,3 arrangement. This probably has its explanation in both electronic and steric effects. Examination of the resonance structures of, for example, the isoxazolinone and oxazolinone systems, shows that in the former compounds the negative charge is placed on a nitrogen atom but in the latter compound on a carbon atom.



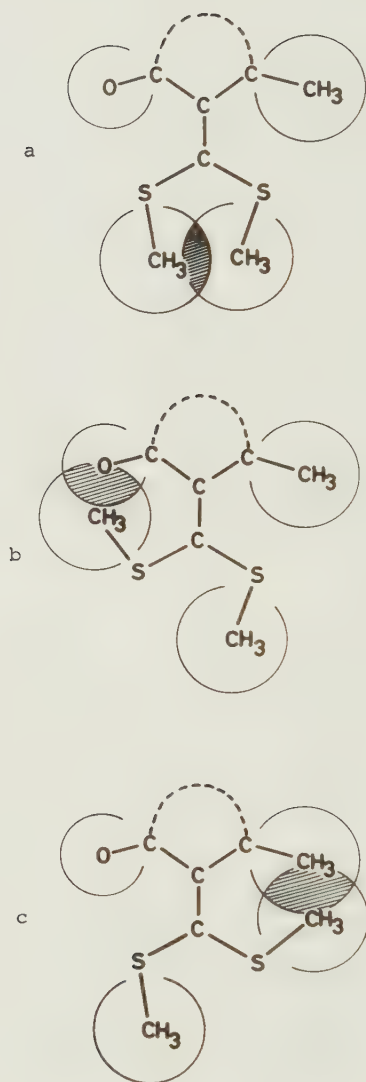


Fig. 14 Illustration of the steric interference in azolinones.

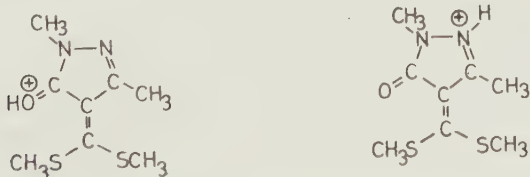
This will lead to an energetically more favourable transition state of the rotational process compared to the initial state in the isoxazolinone system than in the oxazolinone and thus to a lower barrier in the former compounds.

The steric effect is a result of interaction between the methyl group in the 3-position of 29, 30 and 33, and the bis-(methylthio)methylene group. From model studies it can be concluded that appreciable steric interaction is present in all of the conformers a-c (Fig. 14). This leads to an increase of the energy of the initial state and to a lower barrier. On the other hand the oxazolinone and thiazolinone systems may assume a conformation without steric strain.

VI.6 Effect of acid and solvent

Very little is known about acid catalysis on rotational barriers around carbon-carbon double bonds in push-pull substituted ethylenes. Huisgen *et al.*^{79,80} have found that cis-trans isomerization of enamine- β -carbonic esters is catalyzed by acids. As strong catalytic effect of traces of trifluoroacetic acid on the rotational barrier in ketene aminaes was observed by Kessler,⁷⁸ but he reports no quantitative data.

The heterocyclic systems studied in this work exhibit two basic centers, the nitrogen atom of pyridine type and the carbonyl oxygen atom.



Either of these protonated forms, or both of them together, may be responsible for the catalytic effect on the rotation. A decrease of the barrier on protonation on either of these atoms is understandable in view of the absence of charge

separation in the transition state. In conjunction with this it is surprising that such a large negative entropy of activation was obtained for the catalyzed process. The rotation of the nonprotonated species involves charge separation, which should lead to a more strongly solvated transition state, whereas in the protonated molecule the change in polarity between the initial state and the transition state is much less. Thus a more negative entropy of activation should be expected for the uncatalyzed process. $\Delta S^\ddagger$ values in the range -17 to -24 e.u. have previously been obtained for rotations around carbon-carbon double bonds.⁶

The characteristic sigmoidal dependence of the barrier on concentration observed for 29 in ODC and benzonitrile and for 31 in benzonitrile is not completely understood. Under the assumption that the azolinone reacts with the acidic impurity to give a protonated species and that the rate of rotation is much higher for this cation than for the neutral molecule, a successive increase of the barrier on dilution should be expected according to the Ostwald dilution law. With certain values of the equilibrium constant, the rate constants of the protonated and unprotonated forms and the ratio between the concentrations of azolinone and catalyst, a sigmoidal dependence of $\Delta G^\ddagger$ on the concentration of the substrate could be obtained by calculations, but the shape of the experimental curve could not be reproduced. However, the calculations included many unknown parameters and, in particular, the temperature dependence of these parameters is uncertain.

The $\Delta G_{TC}^\ddagger$ value for 29 is about 2 kcal/mol lower in benzonitrile than in ODC and the same behavior was observed for the other systems. This is an indication that the rotational barriers of these compounds are strongly dependent upon the nature of the solvent. The $\Delta G^\ddagger$ values for 29 in three solvents are summarized in Table XXVII. An analogous decrease of the barrier with increasing polarity of the solvent was also observed for ketene amins, ⁷⁸ calicene⁶⁴ and 6-dimethylamino-fulvene.^{65,66} This is in harmony with the assumed polar transition state for the rotation, the transition state being better stabilized in a polar than in a nonpolar medium.

Table XXVII. Effect of solvent on $\Delta G_{T_c}^*$ for 29 (1 M).

Solvent	Dipole moment of solvent (D) ^a	$\Delta G_{T_c}^*$
1,4-Dichlorobenzene	0	22.1
1,2-Dichlorobenzene	2.27	21.5
Benzonitrile	3.90	19.6

^a From Ref. 81.

VI.7 Molecular orbital calculations

The main part of the rotational barrier in these molecules can be ascribed to a difference in π -electron energy between the initial state and the transition state. For this reason the Pariser-Parr-Pople (PPP) approximation⁸²⁻⁸⁴ has been used. In these calculations, only the π -electrons may be explicitly taken into account (σ - π separation). The PPP method is based on the Roothaan equations,⁸⁵ simplified by the Zero Differential Overlap (ZDO) approximation.⁸⁶ The Fock matrix elements in the PPP approximation are given by equations (11a) and (11b):

$$F_{\mu\mu} = H_{\mu\mu}^{\text{core}} - 1/2 q_{\mu} \gamma_{\mu\mu} + \sum_{\lambda} q_{\lambda} \gamma_{\mu\lambda} \quad (11a)$$

$$F_{\mu\nu} = \beta_{\mu\nu} - 1/2 p_{\mu\nu} \gamma_{\mu\nu}; \mu \neq \nu \quad (11b)$$

In these equations, the symbols have the following meaning:

H^{core} = the core Coulomb integral

$$q_{\mu} = 2 \sum_i c_{i\mu}^2 = \pi\text{-electron density at atom } \mu$$

$$p_{\mu\nu} = 2 \sum_i c_{i\mu} c_{i\nu} = \pi\text{-bond order between atoms } \mu \text{ and } \nu$$

The c 's are LCAO wave function coefficients.

$$\gamma_{\mu\mu} = \text{one-center repulsion integrals}$$

$$\gamma_{\mu\lambda} \gamma_{\mu\nu} = \text{two-center repulsion integrals}$$

$$\beta_{\mu\nu} = \text{resonance integrals}$$

The total π -electron energy is given by (12):

$$\begin{aligned} E_{\pi} = & \sum_{\mu} q_{\mu} H_{\mu\mu}^{\text{core}} + 2 \sum_{\mu < \nu} p_{\mu\nu} \beta_{\mu\nu} + 1/4 \sum_{\mu} q_{\mu}^2 \gamma_{\mu\mu} + \\ & + \sum_{\mu < \nu} \sum (q_{\mu} q_{\nu} - 1/2 p_{\mu\nu}^2) \gamma_{\mu\nu} \end{aligned} \quad (12)$$

According to the Goeppert-Mayer and Sklar approximation,⁸⁷ and with neglect of penetration integrals, the core Coulomb integrals will have the form:

$$H_{\mu\mu}^{\text{core}} = U_{\mu\mu} - \sum_{\nu \neq \mu} n_{\nu} \gamma_{\mu\nu} \quad (13)$$

where n_{ν} is the number of electrons contributed by the atomic orbital ν . $U_{\mu\mu}$ is treated as the negative ionization potential of atom μ ($-I_{\mu}$) in the appropriate valence state.

For the determination of the Fock matrix elements, one starts with an approximate electron distribution and iterates the calculations until self consistency is attained. Some of the integrals are treated as standard parameters.

Parametrization

The core Coulomb integrals were obtained from equation (14).

$$H_{\mu\mu}^{\text{core}} = -I_{\mu} - \sum_{\nu \neq \mu} n_{\nu} \gamma_{\mu\nu} \quad (14)$$

For the one-center repulsion integrals the formula

$$\gamma_{\mu\mu} = I_{\mu} - A_{\mu} \quad (15)$$

was proposed by Pariser.⁸⁸ A_{μ} is the electron affinity of atom μ . The ionization potentials and the one-center integrals are summarized in Table XXVIII.

Table XXVIII. Parameters for the PPP calculations.

Atom	I_{μ} (eV)	$\gamma_{\mu\mu}$ (eV)	Ref.
C	11.42	10.84	89
$\dot{\text{N}}$	14.12	12.34	90
$\ddot{\text{N}}$	28.71	16.75	90
$\dot{\text{O}}$	16.86	15.23	90
$\ddot{\text{O}}$	26.73	14.58	91
$\ddot{\text{S}}$	20.40	10.84	92

The two-center repulsion integrals, $\gamma_{\mu\nu}$, were calculated according to the approximation given by Mataga and Nishimoto⁹³:

$$\gamma_{\mu\nu} = \frac{14.40}{r_{\mu\nu} + k_{\mu\nu}} \text{ eV} \quad (16)$$

In this equation, $r_{\mu\nu}$ is the internuclear distance between atoms μ and ν and $k_{\mu\nu}$ is defined by

$$k_{\mu\nu} = \frac{28.40}{\gamma_{\mu\mu} + \gamma_{\nu\nu}} \quad (17)$$

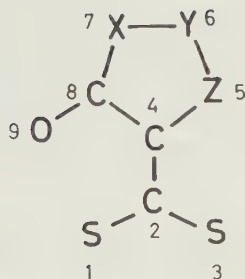
The core resonance integrals $\beta_{\mu\nu}$ were calculated by means of the expression first proposed by Mulliken⁹⁴ and then modified to a relationship of the type (18).⁹⁵

$$\beta_{\mu\nu} = - \frac{S_{\mu\nu}}{1 + S_{\mu\nu}} \cdot \frac{I_{\mu} + I_{\nu}}{2} \quad (18)$$

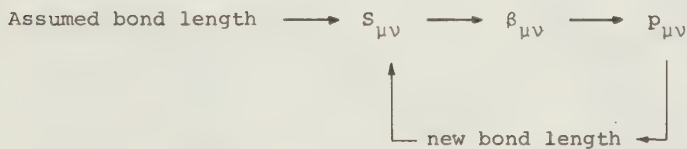
Here $S_{\mu\nu}$ are the overlap integrals, evaluated according to Mulliken et al.⁹⁶

VI.8 Geometries

Experimental determinations of bond lengths and bond angles for these azolinone ring systems were not available, and consequently the geometries had to be constructed from assumed bond lengths by a procedure in which the bond angles in the ring were changed until reasonable values were obtained. The bond lengths C(4)-C(8) and C(8)-O(9) and the angles S(1)-C(2)-S(3), S(1)-C(2)-C(4), C(2)-C(4)-C(8), C(4)-C(8)-O(9) and Z(5)-C(4)-C(8) were kept the same for all the systems.



Since it was observed that the calculated barriers were very sensitive to the S(1,3)-C(2) and C(2)-C(4) bond lengths, the geometry of this group was made self-consistent by an iterative process⁹⁷:



The bond lengths were calculated from the bond orders by formulas (19) and (20)⁹⁸:

$$R_{CS} = 1.80 - 0.23 p_{CS} \quad (19)$$

$$R_{CC} = 1.51 - 0.18 p_{CC} \quad (20)$$

The iterations were continued until convergence was obtained within two decimal places. The bond lengths and bond angles used in the calculations are given in Fig. 15.

The bond lengths and bond angles in the phenyl groups were 1.40 Å and 120°, respectively. The phenyl-azolinone pivot bond lengths were 1.40 Å for 31 (C-N) and 1.43 Å for 35, 36 and 37 (C-C).

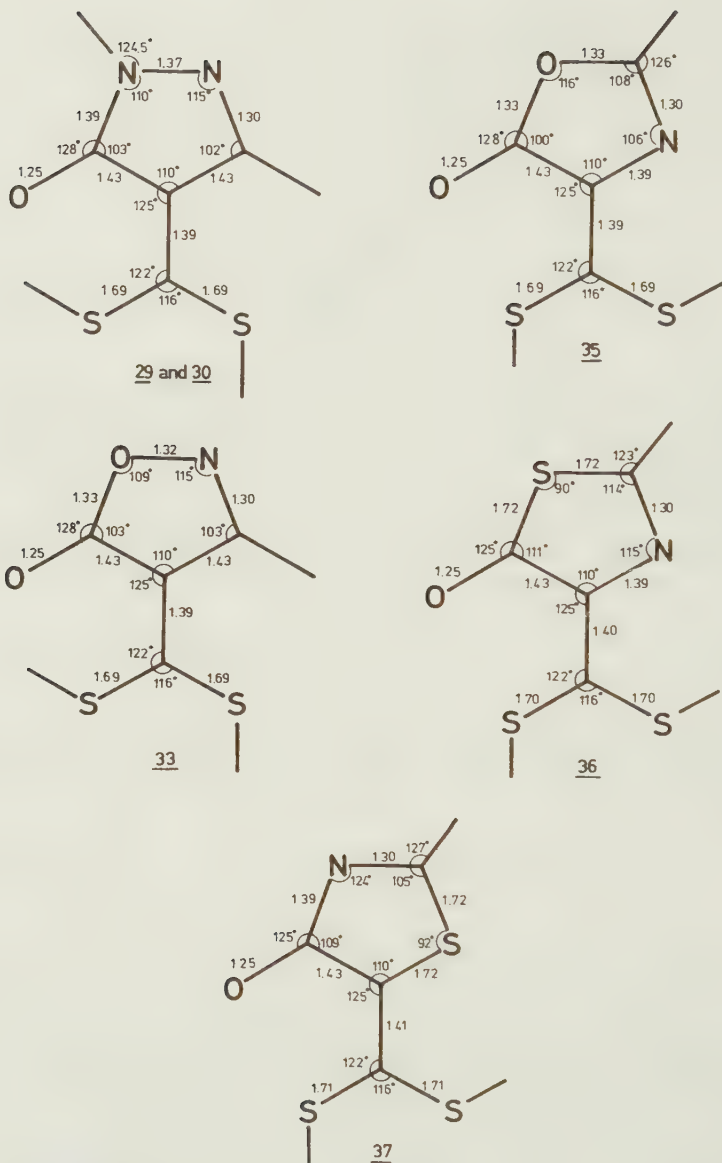


Fig. 15. Geometries of the azolinones used in the PPP calculations.

In the 90°-twisted molecules, all bond lengths and bond angles were the same as in the initial state except for the S(1,3)-C(2) and C(2)-C(4) bond lengths. The value obtained for the S(1,3)-C(2) bond by the iterative process was 1.64 Å for all the molecules. The C(2)-C(4) bond length will be discussed in the following section.

VI.9 Calculation of rotational barriers

The rotational barriers were calculated according to equation (21):

$$\Delta E_{\text{tot}} = \Delta E_{\pi} + \Delta E_{\text{core}} \quad (21)$$

In this expression, $\Delta E_{\pi} = E_{\pi}(90^{\circ}) - E_{\pi}(0^{\circ})$ is the difference in π -electron energy between the transition state (the bis-(methylthio)methylene group twisted 90° out of the plane of the ring) and the initial state, and $\Delta E_{\text{core}} = E_{\text{core}}(90^{\circ}) - E_{\text{core}}(0^{\circ})$ is the difference in core repulsion energy between the transition state and the initial state.⁹⁹

The repulsion between the positively charged core atoms (E_{core}) was represented by the equation

$$E_{\text{core}} = \sum_{\mu < \nu} n_{\mu} n_{\nu} \gamma_{\mu\nu} \quad (22)$$

In this method, variations in the values of the two-electron integrals will influence the values of the π -electron energy (E_{π}) and the repulsion energy (E_{core}) in a similar way.

VI.10 Results of the calculations

The calculated barriers are presented in Table XXIX together with the experimental $\Delta G^{\ddagger}$ values. Only atoms contributing to the π -electron system have been taken into account.

Table XXIX. Calculated barriers and experimental $\Delta G^\ddagger$ values for compounds 29, 30, 33, 35, 36 and 37 (kcal/mol).

Compound	ΔE_π	$-\Delta E_{\text{core}}$	ΔE_{tot}	$\Delta G^\ddagger$
<u>29</u>	49.44	23.19	26.25	21.5
<u>30</u>	57.26	32.05	25.21	18.8
<u>33</u>	48.98	23.32	25.61	18.8
<u>35</u>	60.21	33.51	26.70	>25
<u>36</u>	63.94	35.07	28.87	>25
<u>37</u>	70.93	33.93	37.00	>25

Table XXX. Effect of variation of the C(2)-C(4) bond length in the transition state on the calculated barriers of 29 and 33.

$R[\text{C}(2)-\text{C}(4)]^{\text{TS}}$ (Å)	Calculated barrier (kcal/mol)	
	<u>29</u>	<u>33</u>
1.45	25.95	25.30
1.47	26.25	25.60
1.49	26.55	25.92
1.51	26.85	26.22

Thus hyperconjugation of the methyl groups has been omitted. Since the β -value of the C(2)-C(4) bond in the transition state was fixed at zero, the length of this bond could not be obtained by the iterative process. The barriers for the two compounds 29 and 33 have been calculated with different lengths of this bond. The results are given in Table XXX. The value 1.47 Å was chosen for all compounds in Table XXIX.

Most earlier attempts to calculate barriers to internal rotation concern rotation around carbon-carbon single bonds and carbon-nitrogen single bonds, for which the transition state does not involve charge separation. Barriers in compounds such as benzaldehyde,⁹⁹ biphenyl,^{100,101} nitrobenzene¹⁰² and dimethylamino substituted azoles¹⁰³ have been studied by the PPP method with usually satisfactory results. Gleicher and Arnold¹⁰⁴ carried out PPP calculations on the rotational barrier around the carbon-carbon double bond in calicenes and found energy barriers in the range of 55 to 63 kcal/mol without inclusion of core repulsion energies.

Experimental $\Delta G^\ddagger$ values and calculated barriers may not be compared directly. The proper thermodynamic parameter that should be used is the enthalpy of activation, $\Delta H^\ddagger$. Furthermore, the calculated barriers refer to gas phase values. Very little is known about the difference in barriers in the gas phase and solution of compounds with a zwitterionic transition state. Some experimental data are available for both gas and liquid phases for compounds with a more polar initial state than transition state. Thus the barrier was found to be approximately 2 kcal/mol lower in the gas phase than in the liquid phase both in dimethylnitrosamine¹⁰⁵ and in benzaldehyde.¹⁰⁶ As these molecules involve a more polar initial state than transition state, whereas the reverse is true for polarized ethylenes, a higher barrier in the gas phase might be expected for the latter compounds. This assumption is also supported by the solvent effects.

Finally, the non-bonded interactions have not been taken into account in the calculations. Steric strain is believed to cause some lowering of the barriers in 29, 30 and 33.

In view of the inadequacy of pi electron calculations

for the evaluation of rotational barriers, and in view of the possible sources of errors discussed above, the magnitudes of the barriers measured in this work were surprisingly well accounted for. The order of barriers of compounds for which experimental barriers could be determined is also reasonably well reproduced, and the experimental observation that the oxazolinone and thiazolinone systems have higher barriers is in accordance with the calculations.

It is interesting to note the role of the core repulsion energies. They are indispensable for obtaining realistic magnitudes as well as a realistic order of the barriers. Inclusion of the core repulsions may well reduce the overestimated barrier in calicene calculated by Gleicher and Arnold¹⁰⁴ to a more realistic value.

VI.11 Ultraviolet spectra

Ultraviolet spectra of the azoliones considered in this chapter have been studied and compared to theoretical values obtained from PPP calculations. The results are shown in Table XXXI and in Fig. 16.

The theoretical results were obtained from the calculations used for the initial state of the barrier calculations. Configuration interaction included 16 singly excited configurations with one electron excited from each of the four highest occupied molecular orbitals to the four lowest vacant orbitals.

One factor which must be considered in a comparison of experimental and theoretical values is the shift produced by methyl substitution. This includes both inductive and steric effects, which have not been accounted for in the calculations. The inductive effect of methyl substitution may be either a small bathochromic or a small hypsochromic shift, and since nothing is known about the effects of substitution on nitrogen, sulphur and carbon in the systems under consideration, the overall effect can not be estimated.

The steric effect is the result of interaction between the methyl group in the 3-position of 29, 30 and 33 and the

bis(methylthio)methylene group discussed in section VI.5. The steric strain is probably counteracted by a twist around one or both of the sulphur-carbon (sp^2) bonds. Such a twist of a conjugated system usually gives rise to hypsochromic shifts.

From Table XXXI it can be seen that the different ring systems give characteristic UV spectra. Thus the compounds have their lowest energy maxima at very different wavelengths (369-556 nm in heptane), and the intensities of these bands vary within a wide interval ($\log \epsilon = 1.77-4.45$).

The long wavelength band of 37 has the extinction coefficient 58.5 and should be ascribed to a $n \rightarrow \pi^*$ transition. The band is shifted towards the blue on going from heptane to ethanol, in agreement with the general behavior of $n \rightarrow \pi^*$ bands.⁵⁸⁻⁶⁰ No equivalent band was found for the isomeric thiazolinone 36 nor for any of the other systems.

It has been found¹⁰⁷ that 1,1-bis(alkylthio)ethylenes usually exhibit small bathochromic shifts with increasing polarity of the solvent, indicating that the excited state is slightly more polar than the ground state. This was also found for the isoxazolinones 33 and 34, oxazolinone 35 and thiazolinone 37. However, the long wavelength band of the pyrazolinones 29-32 shows another picture. This band comes at surprisingly high wavelength and is also considerably less intense. Furthermore, its solvatochromatic shift is towards the blue, and the long wavelength band of 29 completely disappears in sulphuric acid. The second band, however, is bathochromically shifted on changing the solvent from heptane to ethanol and is very little affected on going to sulphuric acid.

The calculated maxima are in good agreement with the experimental values except for the long wavelength bands of 29 and 30, for which the theoretical values are in much better agreement with the bands at 326 and 341 nm, respectively. According to the solvent effects and the results from the PPP calculations it can not be excluded that these bands are $n \rightarrow \pi^*$ transitions, even if the intensities are certainly very high. This may be ascribed to sterically induced twisting of the conjugated system, causing the n and π orbitals to mix and thus enhancing the probability of these transitions according

to the Cookson-Wariyar theory.¹⁰⁸ In such a case it is however surprising that this phenomenon is not observed in the isoxazolinones 33 and 34. The bathochromic shifts observed on changing the methyl substituents in both 1- and 3-positions of the pyrazolinones to phenyl are consistent with a qualitative resonance picture. The effect appears to be cumulative.

Table XXXI. Ultraviolet spectra of azolinones.

Compound	Solvent	$\lambda_{\max}$ nm	$\log \epsilon$ (f)	$\lambda_{\max}$ nm	$\log \epsilon$ (f)	$\lambda_{\max}$ nm	$\log \epsilon$ (f)	$\lambda_{\max}$ nm	$\log \epsilon$ (f)
<u>29</u> Obsd	heptane	418	3.52	326	4.16				
	ethanol	406	3.61	329.5	4.10				
	H ₂ SO ₄			329	4.20				
	Calcd			349	0.41	245	0.08		
<u>30</u> Obsd	heptane	438	3.32	341	4.27	256	4.30		
	ethanol	422 sh	3.59	342.5	4.20	250.5	4.23		
	Calcd			350	0.49	280	0.03	275	0.07
<u>31</u> Obsd	heptane	435	3.48	338	3.96	258	3.86		
	ethanol	424	3.66	356	3.99	314	4.04		
	Calcd								
<u>32</u> Obsd	heptane	452	3.41	349	4.03	310	4.06	276	4.27
	Calcd								
<u>33</u> Obsd	heptane	369	4.03	306	3.86				
	ethanol	375	4.05	315	3.80				
	Calcd	367	0.34	252	0.04				
<u>34</u> Obsd	heptane	383	3.99	305	4.05				
	Calcd								

Table XXXI. cont.

Compound	Solvent	$\lambda_{\max}$ nm	$\log \epsilon$ (f)	$\lambda_{\max}$ nm	$\log \epsilon$ (f)	$\lambda_{\max}$ nm	$\log \epsilon$ (f)	$\lambda_{\max}$ nm	$\log \epsilon$ (f)
<u>35</u> Obsd	heptane	385	4.45	288	3.86	261.5	4.06		
	ethanol	390	4.45	285	3.97				
Calcd		408	0.50	301	0.10	297	0.08		
<u>36</u> Obsd	heptane	410	4.30	292	4.13	283	4.13		
	ethanol	407	4.35	283.5	4.24				
Calcd		414	0.50	308	0.01	304	0.20		
<u>37</u> Obsd	heptane	556	1.77	417	4.17	313	4.18	274	4.06
	ethanol	545	1.83	425	4.28	315	4.23	293	0.03
Calcd				413	0.36	304	0.16	272	0.62

sh = shoulder

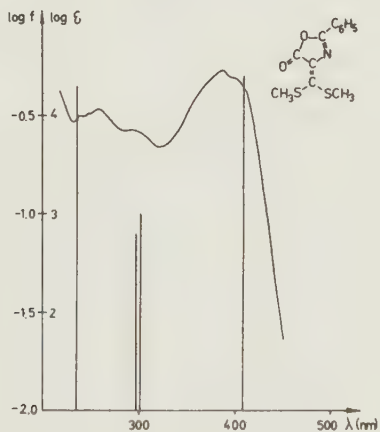
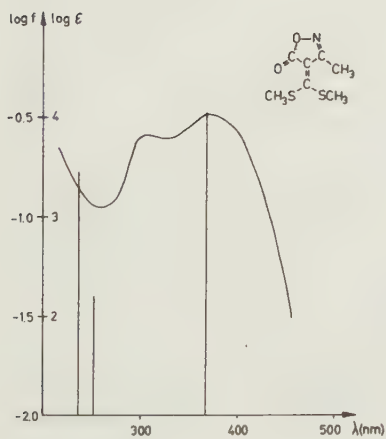
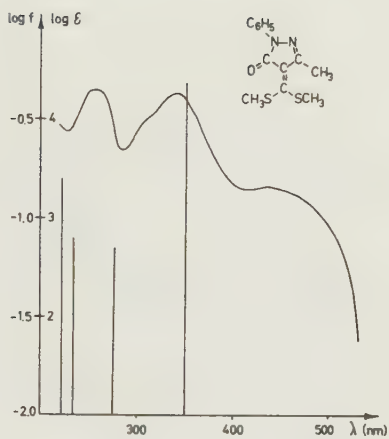
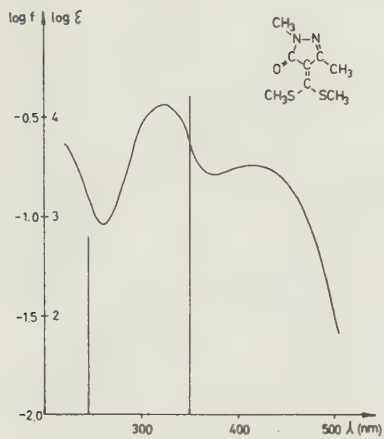


Fig. 16 Experimental (in heptane) and calculated UV spectra.

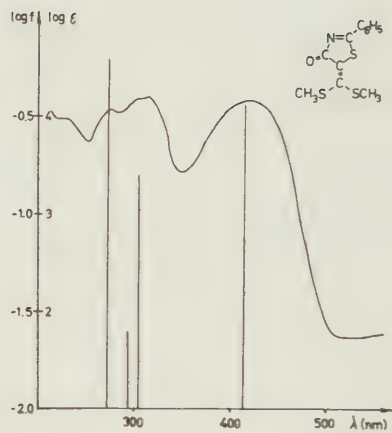
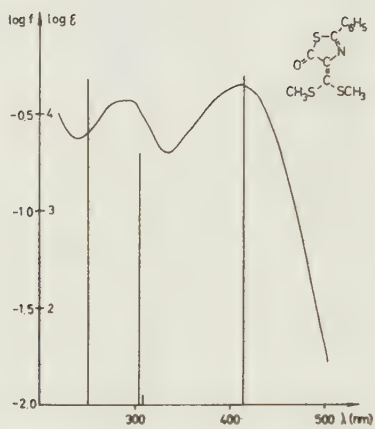


Fig. 16 cont.

VII. EXPERIMENTAL

NMR spectra were recorded on Varian A-60 or A-60A spectrometers equipped with Varian V-6031 variable temperature probes and V-6040 temperature controllers. A few spectra were recorded on a Varian XL-100-15 spectrometer. Chemical shifts were measured by the side-band technique using a HP 200 CD Audio Oscillator. The frequencies were measured with a HP 3734 A Electronic Counter. All shifts are given relative to tetramethylsilane as internal standard. UV spectra were recorded on a Unicam SP 800 B Ultraviolet Spectrophotometer and IR spectra on a Perkin-Elmer Model 221 prism-grating instrument. The program for the PPP calculations was written by Prof. Rolf Manne, University of Bergen, Norway. The calculations were performed on a UNIVAC 1108 computer.

The hydroxyaryldithioesters were prepared according to Gompper, Schmidt and Kutter.⁴

Method A: 0.1 mol of the phenol in question was dissolved in ca. 75 ml of dimethyl sulphoxide (DMSO) and transferred to a 250 ml three necked flask provided with mechanical stirrer, condenser and dropping funnel. To this solution, half of a concentrated water solution of 0.2 mol potassium hydroxide was added, and then 0.05 mol of carbon disulphide over a period of ca. 30 min at 10-20°. Half of the remaining hydroxide (0.05 mol) was added, followed by 0.025 mol of carbon disulphide during 30 min. This operation was repeated with the remaining hydroxide solution and 0.025 mol of carbon disulphide. After 2-3 hrs stirring at 10-20°, the solution was cooled to 5°, treated with 0.1 mol of HCl (concentrated solution) followed by 0.1 mol of dimethyl sulphate (or ethyl bromoacetate). The mixture was allowed to stand over night at room temperature and was then poured onto ca. 200 ml of ice-water.

The work-up will be described individually for each substance under consideration.

Method B: 10.0 g (0.2 mol) of sodium hydride dispersion (50 % in paraffin oil) was added to 50 ml of dry DMSO. The stirred mixture was warmed at 75° for 1 hr under a nitrogen atmosphere, generating a suspension of the sodium salt of the DMSO anion. 25 ml of this suspension was added to 0.1 mol of phenol dissolved in ca. 50 ml of dry DMSO. The temperature was raised to 70° and 0.05 mol of carbon disulphide added dropwise during 15 min. The solution was then cooled in an ice-bath and the procedure was repeated with the residue of the DMSO suspension and an additional 0.05 mol of carbon disulphide. The stirring was continued for one hr, and after cooling in an ice-bath 0.1 mol of HCl was added dropwise. With continued cooling, 0.1 mol of dimethyl sulphate (or ethyl bromoacetate) was added dropwise. The red solution was allowed to stand over night and poured onto 200 ml of ice-water. The products were isolated according to the individual descriptions.

Compounds 1, 2 and 4 have been prepared by Gompper, Schmidt and Kutter.⁴

Methyl 2,4-dihydroxydithiobenzoate (1) was prepared from resorcinol by method A; yield 82 %; mp 102-103°C. Lit. value⁴: 96°C.

Methyl 2-hydroxy-4-methoxydithiobenzoate (2) was prepared from resorcinol by method A, but instead of adding 1 equivalent of acid, direct methylation by 2 equivalents of dimethyl sulphate was performed. Yield 21 %; mp 60.5-61°C. Lit. value⁴: 60°C.

Methyl 2-hydroxy-1-dithionaphthoate (4) was prepared from 2-naphthol by method A; yield 43 %, mp 84.5-86°C. Lit. value⁴: 86°C.

Methyl 4-hydroxy-2-methoxydithiobenzoate (3) was prepared according to method B from 9.0 g (0.072 mol) of resorcinol monomethyl ether and 7.2 ml (0.08 mol) of dimethyl sulphate. The water mixture was extracted with benzene and the combined organic phases were washed with water, dried over MgSO₄ and evaporated. The residue, which crystallized upon scraping, was recrystallized from benzene containing about 40 % ligroin (60-85° fraction), yielding 5.9 g (38 %) of yellow plates, mp

126.5-128°C. Calcd. for $C_9H_{10}O_2S_2$ (214.3): C 50.4; H 4.71; S 29.9. Found: C 49.7; H 4.58; S 29.9.

Methyl 4-hydroxy-1-dithionaphthoate (5) and methyl 1-hydroxy-2-dithionaphthoate (6) were prepared by method B from 28.8 g (0.2 mol) of 1-naphthol and 20 ml (0.2 mol) of dimethyl sulphate. The water mixture was extracted with benzene and the combined organic phases were washed with water, dried over $MgSO_4$ and evaporated. A red oil was obtained. Chromatography on a silica column (800 g, 100-200 mesh) with benzene as eluent gave two well-separated red bands. After evaporation of the solution obtained from the first band and after recrystallization of the residue from benzene-ligroin (1:3), 5.4 g (12 %) of orange crystals was obtained (methyl 1-hydroxy-2-dithionaphthoate, 6), mp 75-77°C.

The second band yielded, after recrystallization from benzene-ligroin (1:2), 8.7 g (19 %) of yellow rods (methyl 4-hydroxy-1-dithionaphthoate 5), mp 113-114°C. Calcd. for $C_{12}H_{10}OS_2$ (234.3): C 61.5; H 4.31; S 27.3. Found for 5: C 61.4; H 4.26; S 27.3. Found for 6: C 61.7; H 4.38; S 27.2.

Ethoxycarbonylmethyl 2,4-dihydroxydithiobenzoate (7) was prepared by method A from 11.0 g (0.1 mol) of resorcinol and 16.7 g (0.1 mol) of ethyl bromoacetate. When the reaction mixture was poured onto ice-water, a yellow crystalline precipitate was formed. The crystals were filtered off, dried on an unglazed porcelain plate and recrystallized from 75 % aqueous ethanol. 16.3 g (60 %) of yellow needles was obtained, mp 137-138°C.

Calcd. for $C_{11}H_{12}O_4S_2$ (272.3): C 48.5; H 4.44; S 23.5. Found: C 48.2; H 4.50; S 23.6.

Ethoxycarbonylmethyl 4-hydroxy-2-methoxydithiobenzoate (8) was prepared from 25.0 g (0.2 mol) resorcinol monomethyl ether and 33.4 g (0.2 mol) of ethyl bromoacetate according to method B. The water mixture was extracted with benzene. The combined organic phases were washed with water, dried over $MgSO_4$ and evaporated. The remainder was chromatographed on a neutral alumina column (800 g) with chloroform and successively increasing amounts of ether as eluent. From an orange band,

10.2 g (18 %) of yellow crystals was obtained after evaporation of the solvent. Recrystallization from benzene-ligroin (1:1), mp 106-107°C.

Calcd. for $C_{12}H_{14}O_4S_2$ (286.3): C 50.3; H 4.92; S 22.4. Found: C 50.8; H 4.97; S 22.3.

Ethoxycarbonylmethyl 2-hydroxy-1-dithionaphthoate (9). This compound was prepared by method A from 28.8 g (0.2 mol) of 2-naphthol and 25 ml (0.22 mol) of ethyl bromoacetate. The water mixture was extracted with benzene and the organic phase was washed with water, dried over $MgSO_4$ and evaporated. The residue, which crystallized upon scraping with a glass rod, was recrystallized from methanol containing ca. 10 % water. 15.1 g (25 %) of yellow prisms was obtained, mp 117.5-118.5°C. Calcd. for $C_{15}H_{14}S_2O_3$ (306.4): C 58.8; H 4.60; S 20.9. Found: C 58.5; H 4.65; S 20.9.

Ethoxycarbonylmethyl 4-hydroxy-1-dithionaphthoate (10) and ethoxycarbonylmethyl 1-hydroxy-2-dithionaphthoate (11) were obtained from 28.8 g (0.2 mol) of 1-naphthol and 25 ml (0.22 mol) of ethyl bromoacetate according to method B. The reaction mixture, poured onto ice-water, was extracted with benzene. The benzene phase was washed with water, dried over $MgSO_4$ and evaporated. The residue was chromatographed on an alumina column. On elution with benzene, a rather rapidly moving yellow band appeared. After evaporation of the solvent and recrystallization of the residue from ligroin (60-85°C), 2.5 g (4 %) of yellow needles was obtained, mp 69-70.5°C (compound 11). The column was then eluted with ether and the residue remaining after evaporation recrystallized from ethanol, yielding 16.8 g (27 %) of orange prisms, mp 118.5-119.5°C (compound 10). Calcd. for $C_{15}H_{14}S_2O_3$ (306.4): C 58.8; H 4.60; S 20.9. Found for 10: C 59.0; H 4.45; S 21.0. Found for 11: C 58.7; H 4.51; S 20.8.

Carboxymethyl 2-hydroxy-1-dithionaphthoate (13) was prepared by method A from 14.4 g (0.1 mol) of 2-naphthol and 10.5 g (0.11 mol) of chloroacetic acid dissolved in a minimum of water and neutralized to pH 5-6 with sodium bicarbonate. The reaction mixture, poured onto water, was acidified to pH 3

with 5 M hydrochloric acid, forming a red deposit of oily crystals. Recrystallization from ethanol containing 10 % water yielded 14.4 g (52 %) of red plates, mp 174-176°C. Calcd. for $C_{13}H_{10}S_2O_3$ (278.3): C 56.1; H 3.63; S 23.0. Found: C 56.2; H 3.63; S 22.8.

Ethoxycarbonylmethyl 3,5-di-tert.-butyl-4-hydroxydithiobenzoate (12) was prepared by method A from 20.6 g (0.1 mol) of 2,6-di-tert.-butyl-phenol and 12 ml (0.1 mol) of ethyl bromoacetate. The water mixture was extracted with benzene and the combined organic phases were washed with water, dried over $MgSO_4$ and evaporated. The residue was recrystallized from 90 % ethanol. 22.5 g (61 %) of red rods was obtained, mp 101-102°C. Calcd. for $C_{19}H_{28}O_3S_2$ (368.5): C 61.9; H 7.65; S 17.4. Found: C 61.8; H 7.73; S 17.5.

Benzyl 3,5-di-tert.-butyl-4-hydroxydithiobenzoate (14) was prepared by method A from 20.6 g (0.1 mol) of 2,6-di-tert.-butyl-phenol and 13.0 g (0.1 mol) of benzyl chloride. A red oil separated from the water phase. The oil crystallized upon scraping with a glass rod. The crystals were filtered off and recrystallized from ethanol, giving 21.1 g (57 %) of red prisms, mp 120-121.5°C. Calcd. for $C_{22}H_{28}OS_2$ (372.5): C 70.9; H 7.57; S 17.2. Found: C 70.3; H 7.44; S 17.4.

2-Hydroxy-N,N- dimethylthiobenzamide (15). 12.2 g (0.1 mol) of salicyclic aldehyde and 5.0 g (0.15 mol) of sulphur were mixed in a round-bottomed flask and warmed to ca. 110°C in an oil bath. Dimethylamine was slowly bubbled through the mixture with occasional stirring for 2 hrs. The resulting thick syrup was poured into ice-water and the solution was neutralized with 5 M HCl and extracted with chloroform. The combined organic phases were washed with water, dried over $MgSO_4$ and evaporated. The residue was chromatographed on a neutral alumina column with benzene as eluent. Evaporation of the main fraction gave a brown oil which crystallized upon scraping in the presence of ligroin. The crystals were dissolved in a warm mixture of benzene and ligroin (2:5) and the solution was placed in a refrigerator after cooling to room temperature. 9.6 g (53 %) of pale yellow crystals was obtained after one

day; mp 65-67°C. Calcd. for $C_9H_{11}NOS$ (181.3): C 59.6; H 6.12; N 7.72; S 17.7. Found: C 59.8; H 6.20; N 7.70; S 17.9.

4-Hydroxy-N,N-dimethylthiobenzamide (16). 12.2 g (0.1 mol) of p-hydroxybenzaldehyde and 5.0 g (0.15 mol) of sulphur were mixed in a round-bottomed flask and warmed to ca. 110°C in an oil bath. Dimethylamine was slowly bubbled through the mixture for 2 hrs. The still warm reaction mixture was poured onto ice-water and the solution was neutralized with 5 M HCl and extracted with chloroform. The combined organic phases were washed with water, dried over $MgSO_4$ and evaporated. The residue was chromatographed on a neutral alumina column with acetone as eluent. Brown crystals were obtained by evaporation of the fractions from the main band. Recrystallization from 80 % ethanol gave 4.0 g (22 %) of brown yellow prisms, mp 166-168°C. Calcd. for $C_9H_{11}NOS$ (181.3): C 59.6; H 6.12; N 7.70; S 17.7. Found: C 59.5; H 6.15; N 7.61; S 17.7.

3,5-Di-tert.-butyl-4-hydroxy-N,N-dimethylthiobenzamide (17).

6.0 g (16 mmol) of ethoxycarbonylmethyl 3,5-di-tert.-butyl-4-hydroxydithiobenzoate (12) was refluxed with 2 equivalents of dimethylamine in ca. 60 ml of benzene. After 2 hrs, the starting material had been consumed (thin layer chromatography). The solution was evaporated and the remaining crystals were recrystallized from ethanol, giving 4.1 g (86 %) of pale yellow plates, mp 163-164°C. Lit. value¹⁰⁹: 163.5-164.5°C. Calcd. for $C_{17}H_{27}NOS$ (293.5): C 69.6; H 9.27; N 4.77; S 10.9. Found: C 69.3; H 9.17; N 4.84; S 10.9.

2,4-Dihydroxy-N,N-dimethylthiobenzamide (18). 1.0 g (0.04 mol)

of ethoxycarbonylmethyl 2,4-dihydroxydithiobenzoate (7) and 2 equivalents of dimethylamine were refluxed in 100 ml of benzene for 2 hrs. 70 ml of the solvent was distilled off, giving a yellow precipitate which was filtered off (9.0 g). The crystals were recrystallized from acetone giving 6.7 g (84 %) of pale yellow crystals, mp 123-125°C. Calcd. for $C_9H_{11}NO_2S$ (197.3): C 54.8; H 5.63; N 7.10; S 16.3. Found: C 54.8; H 5.76; N 7.26; S 16.1.

4-Hydroxy-2-methoxy-N,N-dimethylthiobenzamide (19). a) 3.0 g (0.01 mol) of ethoxycarbonylmethyl 4-hydroxy-2-methoxydithiobenzoate (8) and 1.5 equivalent of dimethylamine were refluxed in 25 ml of benzene for 2.5 hrs. After ca. 1 hr another equivalent of dimethylamine was added. The solution was evaporated and the residue was chromatographed on a silica column with benzene and increasing amounts of ether as eluent. Recrystallization of the main fractions from 70 % ethanol yielded 1.2 g (54 %) of pale yellow prisms, mp 143-144°C. Calcd. for $C_{10}H_{13}NO_2S$ (211.3): C 56.8; H 6.20; N 6.63; S 15.2. Found: C 57.1; H 6.21; N 6.54; S 15.4.

b) 2.5 g (0.02 mol) of resorcinol monomethyl ether and 3.0 g (0.022 mol) of $AlCl_3$ were dissolved in ca. 50 ml of 1,2-dichloroethane. 2.5 g (0.02 mol) of N,N-dimethylthiocarbamyl chloride dissolved in 5 ml of 1,2-dichloroethane was added dropwise with stirring and cooling in ice-water. The solution was then allowed to stand at room temperature for 1 hr and finally warmed at 40°C for another 15 min. The mixture was hydrolyzed with cold sodium bicarbonate solution, extracted with ether and evaporated. The residue was chromatographed on a silica column with benzene and increasing amounts of ether as eluent. The product was recrystallized from 70 % ethanol. Yield: 1.9 g (45 %); mp 144-145°C.

2-Hydroxy-4-methoxy-N,N-dimethylthiobenzamide (20). 6.0 g (0.04 mol) of 2-hydroxy-4-methoxybenzaldehyde and 2.0 g (0.062 mol) of sulphur were mixed in a round-bottomed flask which was kept in an oil bath at ca. 110°C. Dimethylamine was bubbled through the mixture for 2½ hrs with occasional stirring. The resulting thick syrup was poured onto ice-water while still warm. The solution was neutralized with 5 M HCl and extracted with ether. The combined organic phases were washed with water, dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica column with benzene as eluent. Evaporation of the main fractions gave a yellow oil which was distilled under vacuum. Yield: 2.8 g (34 %); bp 168-174°C/0.6 mm Hg. Calcd. for $C_{10}H_{13}NO_2S$ (211.3): C 56.8;

H 6.20; N 6.63; S 15.2. Found: C 56.5; H 6.17; N 6.52; S 15.3.

2,4-Dimethoxy-N,N-dimethylthiobenzamide (21) was prepared according to Viola, Scheithauer and Mayer¹⁴ from 2.8 g (0.02 mol) of resorcinol dimethyl ether and 2.5 g (0.02 mol) of N,N-dimethylthiocarbamyl chloride. Yield: 2.4 g (53 %); mp 91-92°C. Lit. value¹⁴: 91-92.5°C.

2-Methoxy-N,N-dimethylbenzamide. 30.5 g (0.2 mol) of *o*-methoxybenzoic acid and 40 g (0.34 mol) of thionyl chloride were refluxed for 2 hrs. The solution was evaporated and the residue was dissolved in 100 ml of dioxane and transferred to an Erlenmeyer flask. 0.4 mol of dimethylamine in ca. 100 ml of benzene was added in portions, with cooling and shaking. The solution was allowed to stand over night and was then evaporated. The residue was poured onto ice-water and made basic with 5 M NaOH solution. The solution was extracted with chloroform and the combined organic phases were dried over CaCl₂ and evaporated. A brown liquid was obtained which was distilled under vacuum; bp 112-116°C/0.5 mm Hg. 21.8 g (61 %) of a viscous and colourless liquid was obtained which crystallized upon scraping, mp 72-73°C. Lit. value¹¹⁰: 74-75°C.

2-Methoxy-N,N-dimethylthiobenzamide (22). 15.0 g (0.084 mol) of 2-methoxy-N,N-dimethylbenzamide and 15 g (0.067 mol) of P₄S₁₀ were refluxed with stirring in 110 ml of dioxane for 4 hrs. The reaction mixture was poured onto ice-water. Benzene was added and the layers were separated. The aqueous phase was extracted with benzene and the combined organic layers were washed several times with water, dried over CaCl₂ and evaporated. The residue was distilled in vacuo; bp 145-155°C/0.5 mm Hg. 9.4 g (57 %) of a yellow, thick liquid was obtained. Calcd. for C₁₀H₁₃NOS (195.3): C 61.5; H 6.71; N 7.17; S 16.4. Found: C 59.9; H 6.58; N 7.05; S 16.8.

2-Hydroxy-N,N-dimethyl-1-thionaphthamide (23). 2.5 g (8.1 mmol) of ethoxycarbonylmethyl 2-hydroxy-1-dithionaphthoate (9) was refluxed with 2 equivalents of dimethylamine in 50 ml of benzene for 5 hrs. After about 2 hrs another equivalent of dimethylamine was added. The benzene solution was poured into 50 ml of water and the mixture was neutralized with 5 M HCl.

The benzene phase was separated and the water was extracted with benzene. The combined organic phases were washed with water, dried over MgSO_4 and evaporated. The remaining oily crystals were recrystallized from 90 % ethanol and then from benzene-ligroin (1:2). 1.1 g (58 %) of light yellow rods was obtained, mp $146-147^\circ\text{C}$. Calcd. for $\text{C}_{13}\text{H}_{13}\text{NOS}$ (231.3): C 67.5; H 5.66; N 6.05; S 13.9. Found: C 67.3; H 5.62; N 5.99; S 13.9.

1-Hydroxy-N,N-dimethyl-2-thionaphthamide (24). 3.5 g (0.011 mol) of ethoxycarbonylmethyl 1-hydroxy-2-dithionaphthoate (11) was refluxed with two equivalents of dimethylamine in benzene for two hrs. The solution was evaporated and the residue crystallized slowly. 1.2 g (52 %) of pale yellow crystals was obtained after recrystallization from ethanol; mp $84-85^\circ\text{C}$. Calcd. for $\text{C}_{13}\text{H}_{13}\text{NOS}$ (231.3): C 67.5; H 5.66; N 6.05; S 13.9. Found: C 68.0; H 5.84; N 5.98; S 14.1.

4-Hydroxy-N,N-dimethyl-1-thionaphthamide (25). 5.0 g (0.016 mol) of ethoxycarbonylmethyl 4-hydroxy-1-dithionaphthoate (10) and two equivalents of dimethylamine in 60 ml of benzene were transferred to a Pyrex tube which was cooled to -78°C and sealed. The tube was heated in a steel tube at 150°C for 18 hrs. The solution was then evaporated and the residue chromatographed on a silica column with benzene containing increasing amounts of ether as eluent. Pale yellow crystals (2.5 g, 66 %) were obtained, which were recrystallized from benzene; mp $168-170^\circ\text{C}$. Calcd. for $\text{C}_{13}\text{H}_{13}\text{NOS}$ (213.3): C 67.5; H 5.66; N 6.05; S 13.9. Found: C 67.6; H 5.66; N 6.13; S 13.7.

N,N-Dimethyl-1-naphthamide. 30.0 g (0.16 mol) of 1-naphthoyl chloride was added in portions to a solution of 0.3 mol of dimethylamine in ca. 100 ml of pyridine cooled in ice-water. The solution was allowed to stand over night at room temperature and was then poured onto ice-water. The resulting homogeneous solution was extracted with ether and the combined organic phases were washed with water, 2 M hydrochloric acid, water again and were dried over calcium chloride and evaporated. The residue was distilled in vacuo yielding 12.5 g (39 %) of colourless liquid, bp $140-143^\circ\text{C}/0.5 \text{ mm Hg}$, mp $62-63^\circ\text{C}$. Lit. value¹¹¹: 62°C .

N,N-Dimethyl-2-naphthamide was prepared as described for N,N-dimethyl-1-naphthamide. Evaporation of the ether extract yielded a crystalline residue which was recrystallized from ethanol containing 25 % water. 17.6 g (56 %) of colourless crystals were obtained, mp 87-88°C. Calcd. for $C_{13}H_{13}NO$ (199.2): C 78.4; H 6.58; N 7.03. Found: C 78.3; H 6.63; N 6.97.

N,N-Dimethyl-1-thionaphthamide (26). 9.0 g (0.045 mol) of N,N-dimethyl-1-naphthamide and 7.0 g (0.031 mol) of P_4S_{10} were refluxed in 100 ml of dioxane for 3 hrs. The solution was then evaporated and the residue was poured into water. Extraction with ether and evaporation of the ether phase yielded a thick red syrup. The liquid was distilled in vacuo yielding 3.9 g (40 %) of yellow liquid which crystallized. Recrystallization from 90 % ethanol gave pale yellow crystals, mp 68.5-70°C. Calcd. for $C_{13}H_{13}NS$ (215.3): C 72.5; H 6.08; N 6.50; S 14.9. Found: C 72.5; H 6.26; N 6.57; S 15.3.

N,N-Dimethyl-2-thionaphthamide (27). 10.0 g (0.05 mol) of N,N-dimethyl-2-naphthamide and 7.0 g (0.031 mol) of P_4S_{10} were refluxed in 100 ml of dioxane over night. The warm solution was filtered and evaporated. A red syrup was obtained which was treated with water. The water mixture was extracted with ether and the combined organic phases were washed with water, dried over calcium chloride and evaporated. Oily crystals were obtained which were recrystallized from 90 % ethanol yielding 2.3 g (21 %) of pale yellow crystals, mp 97-98°C. Calcd. for $C_{13}H_{13}NS$ (215.3): C 72.5; H 6.08; N 6.50; S 14.9. Found: C 72.3; H 5.93; N 6.36; S 15.2.

Bis-methylthio-(2-hydroxy-4-methoxyphenyl)-carbonium methyl sulphate. 0.8 g (3.7 mmol) of methyl 2-hydroxy-4-methoxydi-thiobenzoate (2) was heated with 2.5 ml of dimethyl sulphate for 20 min at 120°C. After cooling to room temperature 25 ml of dry ether was added. The oily product crystallized upon scraping, yielding 1.0 g (78 %) red crystals, mp 97-99°C. Calcd. for $C_{11}H_{16}O_6S_3$ (340.3): C 38.8; H 4.73; S 28.3. Found: C 38.5; H 4.65; S 28.4.

Bis-methylthio-(4-hydroxy-2-methoxyphenyl)-carbonium iodide. 0.9 g (4.2 mmol) of methyl 4-hydroxy-2-methoxydithiobenzoate (3) was refluxed in 4 g of methyl iodide for 30 min and was then treated with several portions of dry ether with scraping. 1.0 g (67 %) of orange crystals were obtained which were recrystallized from acetonitrile; mp 113-115°C (decomp.). Calcd. for $C_{10}H_{13}O_2S_2I$ (356.2): C 33.7; H 3.68; S 18.0. Found: C 33.9; H 3.59; S 17.9.

Bis-methylthio-[2-hydroxynaphthyl-(1)]-carbonium methyl sulphate was prepared according to Gompper et al.⁴

Bis-methylthio-[4-hydroxynaphthyl-(1)]-carbonium methyl sulphate. 3.0 g (10.2 mmol) of methyl 4-hydroxy-1-dithionaphthoate (5) was heated with 5 ml of dimethyl sulphate for 20 min at 120°C. After cooling to room temperature 25 ml of dry ether was added. The oily product, which crystallized upon scraping, was recrystallized from acetonitrile, giving 1.5 g (33 %) of red crystals, mp 195-197°C. Calcd. for $C_{14}H_{16}O_5S_3$ (360.5): C 46.7; H 4.48; S 26.7. Found: C 46.8; H 4.62; S 26.6.

Dimethylamino-methylthio-(3,5-di-tert.-butyl-4-hydroxyphenyl)-carbonium iodide. 3.0 g (10.2 mmol) of 3,5-di-tert.-butyl-4-hydroxy-N,N-dimethylthiobenzamide (17) and 1.7 g (12 mmol) of methyl iodide were refluxed in 25 ml of acetone for 30 min. The solution was allowed to stand at room temperature over night. A precipitate was formed which was filtered off and washed with acetone giving 4.1 g (94 %) of white prisms, mp 212-214°C. Calcd. for $C_{18}H_{30}NOSI$ (435.4): C 49.7; H 6.94; N 3.22; S 7.37. Found: C 49.6; H 6.89; N 3.31; S 7.40.

1,3-Diphenylpyrazolin-5-one, 3-methyl-1-phenylpyrazolin-5-one and 1-methyl-3-phenylpyrazolin-5-one were prepared according to Vogel.¹¹²

1,3-Dimethylpyrazolin-5-one. 9.2 g (0.2 mol) of methylhydrazine was added to a mixture of 26 g (0.2 mol) of ethyl acetate and 200 ml of water. The temperature was raised to 70°C for 45 min and the mixture was efficiently stirred during this time. The water was evaporated and the crystalline residue was sublimed twice yielding 17.0 g (76 %), mp 115-116°C. Lit. value¹¹³: 117°C.

General procedure for the reaction between azolinones, sodium hydride and carbon disulphide (0.05 mol). The calculated amount of sodium hydride dispersion (50 % in paraffin oil) was washed with small amounts of dry benzene in order to remove the oil. Ca. 50 ml of dry benzene was at once added to the flask followed by 0.05 mol of azolinone and 0.055 mol of carbon disulphide. The flask was cooled in an ice-bath, and equipped with dropping funnel, condenser and mechanical stirrer. 30 ml of dimethylformamide was added dropwise with stirring. The colour of the solution rapidly changed to orange or red and gas evolution and foaming could be observed. When the reaction had ceased the ice-bath was removed and the mixture was allowed to stand with stirring at room temperature for one hr, was then cooled to ca. 10°C and 0.11 mol of methyl iodide was added dropwise. After standing one hr at room temperature, the mixture was refluxed for 20 min and was then allowed to stand over night. The dark red solution was poured onto ice-water and the benzene phase was separated. The water phase was extracted with benzene and the combined organic phases were washed with water, dried over calcium chloride and evaporated. The products were isolated according to the individual descriptions.

4-Bis(methylthio)methylene-1,3-dimethylpyrazolin-5-one (29)

was obtained from 5.6 g (0.05 mol) of 1,3-dimethylpyrazolin-5-one. The residue from the evaporated benzene solution, an orange crystalline product, was recrystallized from ligroin, yielding 8.2 g (76 %) of orange plates, mp 86-87°C. Calcd. for $C_8H_{12}N_2OS_2$ (216.3): C 44.4; H 5.59; N 12.9; S 29.6. Found: C 44.0; H 5.36; N 13.0; S 30.0.

4-Bis(methylthio)methylene-3-methyl-1-phenylpyrazolin-5-one

(30) was prepared from 10.5 g (0.06 mol) of 3-methyl-1-phenylpyrazolin-5-one. The product was recrystallized from benzene-ligroin (1:3), yielding 10.0 g (55 %) of red prisms, mp 73-75°C. Lit. value¹¹⁴: 77-78°C. Calcd. for $C_{13}H_{14}N_2OS_2$ (278.3): C 56.1; H 5.07; N 10.1; S 23.0. Found: C 56.3; H 4.91; N 10.2; S 22.8.

4-Bis(methylthio)methylene-1-methyl-3-phenylpyrazolin-5-one (31). This compound was obtained from 8.7 g (0.05 mol) of 1-methyl-3-phenylpyrazolin-5-one. Evaporation of the benzene solution yielded a red oil which crystallized upon scraping in the presence of ligroin. The product was recrystallized from benzene-ligroin (1:5), yielding 7.1 g (51 %) of red plates, mp 107-108°C. Calcd. for $C_{13}H_{14}N_2OS_2$ (278.3): C 56.1; H 5.07; N 10.1; S 23.0. Found: C 55.8; H 4.99; N 10.1; S 22.9.

4-Bis(methylthio)methylene-1,3-diphenylpyrazolin-5-one (32) was prepared from 23.1 g (0.1 mol) of 1,3-diphenylpyrazolin-5-one. The evaporated benzene solution yielded a red oil which crystallized upon scraping in the presence of ligroin. Recrystallization from benzene-ligroin (1:3) yielded 21.1 g (62 %) of red prisms, mp 146-147°C. Calcd. for $C_{18}H_{16}N_2OS_2$ (340.4): C 63.5; H 4.73; N 8.23; S 18.8. Found: C 63.3; H 4.62; N 8.19; S 18.9.

3-Phenylisoxazolin-5-one was prepared according to Hantzsch.¹¹⁵

3-Methylisoxazolin-5-one was prepared according to Katritzky, Øksne and Boulton.¹¹⁶

4-Bis(methylthio)methylene-3-methylisoxazolin-5-one (33). This compound was obtained from 6.1 g (0.06 mol) of 3-methylisoxazolin-5-one. The DMF should be added very carefully since otherwise the reaction gets too violent. Evaporation of the benzene phase gave a yellow crystalline product which was recrystallized from ethanol or benzene-ligroin (1:5). Yield: 6.0 g (50 %); mp 92-93°C. Calcd. for $C_7H_9NO_2S_2$ (203.3): C 41.4; H 4.48; N 6.89; S 31.5. Found: C 41.7; H 4.67; N 6.94; S 31.7.

4-Bis(methylthio)methylene-3-phenylisoxazolin-5-one (34) was prepared from 8.1 g (0.05 mol) of 3-phenylisoxazolin-5-one. After evaporation of the benzene solution, the remaining oil crystallized upon scraping in the presence of ligroin. The crystals were recrystallized from ethanol, yielding 6.5 g (49 %) of yellow prisms, mp 139-140.5°C. Calcd. for $C_{12}H_{11}NO_2S_2$ (265.3): C 54.3; H 4.18; N 5.27; S 24.2. Found: C 54.7; H 4.24; N 5.27; S 24.4.

4-Bis(methylthio)methylene-2-phenyloxazolin-5-one (35) and S-methyl 5-methylthio-2-phenyloxazole-4-carbothioate (41).

It was intended to prepare 35 from 8.1 g (0.05 mol) of 2-phenyloxazolin-5-one according to the general description above. Evaporation of the benzene solution yielded a pale yellow crystalline product. Recrystallization from ethanol gave 2.7 g (20 %) of nearly white needles (41), mp 144-144.5°C, and a yellow mother liquor. The mother liquor was evaporated and the remaining yellow crystals were recrystallized from benzene-ligroin (1:1), yielding 1.2 g (9 %) of bright yellow needles (35), mp 119-120°C. Lit. value¹⁵ for 35 119-120°C and for 41¹⁶ 145-146°C. Calcd. for C₁₂H₁₁NO₂S₂ (265.3): C 54.4; H 4.18; N 5.27; S 24.2. Found for 35: C 54.2; H 4.09; N 5.15; S 24.4 and for 41: C 54.5; H 4.33; N 5.33; S 24.3.

2-Phenylthiazolin-5-one was prepared from carboxymethyl di-thiobenzoate (prepared according to Holmberg¹¹⁷) by the procedure described by Jepson, Lawson and Lawton.¹¹⁸

4-Bis(methylthio)methylene-2-phenylthiazolin-5-one (36) was prepared from 4.0 g (0.022 mol) of 2-phenylthiazolin-5-one according to the general description above. Evaporation of the benzene solution gave a dark red crystalline product which was recrystallized from benzene-ligroin (3:7), yielding 2.5 g (39 %) of red-brown rods, mp 106-107°C. Lit. value¹⁵: 106.5-107°C.

2-Phenylthiazolin-4-one was prepared according to Jensen and Crossland.¹¹⁹

5-Bis(methylthio)methylene-2-phenylthiazolin-4-one (37) was prepared from 3.0 g (0.017 mol) of 2-phenylthiazolin-4-one. Evaporation of the benzene solution gave a dark red oil which could not be induced to crystallize. The oil was subjected to chromatography on a neutral alumina column with benzene and increasing amounts of ether as eluent. A yellow unidentified band was eluted rapidly while a darker band was eluted with an ether concentration of ca. 10 %. Dark red crystals were obtained from this band and were recrystallized from ethanol or from benzene-ligroin (1:5); yield 1.0 (18 %), mp 100-101.5°C.

Calcd. for $C_{12}H_{11}NOS_3$ (281.4): C 51.2; H 3.94; N 4.98; S 34.2.
Found: C 51.3; H 3.94; N 5.07; S 34.3.

2-Dimethylaminothiazolin-4-one was a gift from Eva Åkerblom, Pharmacia AB, Uppsala. Its preparation has been described.¹²⁰

5-Bis(methylthio)methylene-2-dimethylaminothiazolin-4-one (38) was obtained from 1.4 g (0.01 mol) of 2-dimethylaminothiazolin-4-one according to the general description above. From the evaporated benzene solution, yellow, oily crystals were obtained which were washed with petroleum ether and recrystallized from benzene-ligroin (2:3). 1.6 g (64 %) of yellow prisms were obtained, mp 112-113.5°C. Calcd. for $C_8H_{12}N_2OS_3$ (248.4): C 38.7; H 4.87; N 11.3; S 38.7. Found: C 38.9; H 4.91; N 11.3; S 38.7.

5-Bis(methylthio)methylene-3-methylthiazolidin-2-thion-4-one (39) was prepared from 14.7 g (0.1 mol) of 3-methylthiazolidin-2-thion-4-one. The dark oil that was obtained from the evaporated benzene solution was chromatographed on an alumina column. Evaporation of the first eluted band yielded 10.0 g (40 %). Recrystallization from ethanol gave yellow plates, mp 118.5-119.5°C. Lit. value¹²¹: 115°C. Calcd. for $C_7H_9NOS_4$ (251.5): C 33.4; H 3.62; N 5.57; S 51.0. Found: C 33.3; H 3.32; N 5.71; S 51.3.

5-Bis(methylthio)methylene-3-phenylthiazolidin-2-thion-4-one (40). 2.0 g (0.01 mol) of 3-phenylthiazolidin-2-thion-4-one was dissolved in 25 ml abs. ethanol. 0.5 g (0.022 mol) of sodium and 0.76 g (0.01 mol) of carbon disulphide were each divided into three portions which were alternately added to the cooled ethanol solution. After each portion the mixture was stirred for 15 min. The red solution was allowed to stand for 2 hrs at room temperature and was then furnished with 2 ml (0.022 mol) of dimethyl sulphate. The mixture was stirred for 4 hrs and was then poured onto ice-water. The water mixture was extracted with chloroform and the combined organic phases were washed with water, dried over calcium chloride and evaporated. The residue was subjected to chromatography on an alumina column with benzene as eluent. Evaporation of the yellow main band yielded 0.35 g (11 %) of yellow prisms, mp

152-154°C. Calcd. for $C_{12}H_{11}NOS_4$ (313.5): C 46.0; H 3.54; N 4.47; S 40.9. Found: C 46.4; H 3.62; N 4.52; S 39.8.

4-[Bis(dimethylamino)methylene]-1,3-dimethylpyrazolin-5-one (42). 1.5 g (7 mmol) of 4-bis(methylthio)methylene-1,3-dimethylpyrazolin-5-one was dissolved in 7 ml of benzene. The solution was treated with 7 ml of a benzene solution containing 15 mmol of dimethylamine and was then refluxed for 30 min. The solution was evaporated and the residue was chromatographed on an alumina column which was eluted with chloroform. One fraction gave a crystalline product which was recrystallized from ethanol, yielding 0.5 g (34 %) of pale yellow and hygroscopic crystals, mp 135-137°C. Calcd. for $C_{10}H_{18}N_4O$ (210.2): C 57.1; H 8.61; N 26.6. Found: C 57.4; H 8.50; N 26.6.

4-(Dimethylamino-methylthiomethylene)-1,3-diphenylpyrazolin-5-one (43). 4.0 g (0.012 mol) of 4-bis(methylthio)methylene-1,3-diphenylpyrazolin-5-one was dissolved in 10 ml of benzene. The solution was treated with 10 ml of a dimethylamine solution in benzene containing 0.013 mol of dimethylamine. The intensely red colour nearly instantaneously changed to yellow. After 15 min all starting material had been consumed (thin layer chromatography) and the solution was evaporated. The residue, a thick syrup, was extracted with boiling ligroin (85-110°C) several times. The combined ligroin solutions were allowed to cool to room temperature and were then cooled to -20°C in a refrigerator. Small yellow crystals were formed which were filtered and stored in a vacuum desiccator. Yield: 1.5 g (38 %); mp 76-79°C. Calcd. for $C_{19}H_{19}N_3OS$ (337.5): C 67.6; H 5.69; N 12.4; S 9.51. Found: C 67.7; H 5.74; N 12.3; S 9.30.

4-(Dimethylamino-methylthiomethylene)-3-phenylisoxazolin-5-one (44). 1.0 g (3.8 mmol) of 4-bis(methylthio)methylene-3-phenylisoxazolin-5-one was refluxed with 4.3 mmol of dimethylamine in ca. 10 ml of benzene. The reaction was followed by thin layer chromatography. After 20 min all the starting material had been consumed. The solution was evaporated, yielding a pale yellow crystalline product which was recrystallized from ethanol. 0.7 g (71 %) of pale yellow prisms were obtained, mp

186.5-188°C. Calcd. for $C_{13}H_{14}N_2O_2S$ (262.3): C 59.5; H 5.38;
N 10.7; S 12.2. Found: C 59.2; H 5.60; N 10.7; S 12.3.

REFERENCES

1. Binsch, G. in "Topics in Stereochemistry", Vol. 3, Eliel, E.L. and Allinger, N.L., Eds., Interscience Publishers, John Wiley, New York, 1968, p. 132.
2. Sutherland, I.O. in "Annual Reports on NMR Spectroscopy", Vol. 3, Mooney, E.F., Ed., Academic Press, London and New York, 1971, p. 71.
3. Kalinowski, H.-O. and Kessler, H. in "Topics in Stereochemistry", Vol. 7, Eliel, E.L. and Allinger, N.L., Eds., Interscience Publishers, John Wiley, New York, 1973, p. 295.
4. Gompfer, R., Schmidt, R.R. and Kutter, E., Ann. Chem. 684, 37 (1965).
5. Gompfer, R. and Töpfl, W., Chem. Ber. 95, 2861 (1962).
6. Sandström, J. and Wennerbeck, I., Acta Chem. Scand. 24, 1191 (1970).
7. Jensen, K.A. and Henriksen, L., Acta Chem. Scand. 22, 1107 (1968).
8. Ericsson, E., Sandström, J. and Wennerbeck, I., Acta Chem. Scand. 24, 3102 (1970).
9. Walter, W. and Voss, J. in "The Chemistry of Amides", Patai, S. and Zabicky, J., Eds., Interscience Publishers, John Wiley, London, 1970.
10. Holmberg, B., Arkiv Kemi, Mineral. Geol. Ser. A, 17, 23 (1944).
11. Kindler, K., Ann. Chem. 464, 278 (1928).
12. Asinger, F., Schäfer, W., Halcour, K., Sans, A. and Triem, H., Angew. Chem. 75, 1050 (1963).
13. Jensen, K.A. and Pedersen, C., Acta Chem. Scand. 15, 1087 (1961).
14. Viola, H., Scheithauer, S. and Mayer, R., Chem. Ber. 101, 3517 (1968).
15. Brown, R.F.C., Rae, I.D. and Sternhell, S., Aust. J. Chem. 18, 61 (1965).
16. Brown, R.F.C., Rae, I.D., Shannon, J.S., Sternhell, S. and Swan, J.M., Aust. J. Chem. 19, 503 (1966).

17. Stewart, W.E. and Siddall, III, T.H.,
Chem. Rev. 70, 517 (1970).
18. Block, F., Phys. Rev. 76, 460 (1946).
19. Hahn, E.L. and Maxwell, D.E., Phys. Rev. 88, 1070 (1952).
20. McConnell, H.M., J. Chem. Phys. 28, 430 (1958).
21. Allerhand, A., Gutowsky, H.S., Jonas, J. and Meizner, R.A.,
J. Am. Chem. Soc. 88, 3185 (1966).
22. Gutowsky, H.S. and Holm, C.H.,
J. Chem. Phys. 25, 1228 (1956).
23. Kost, D., Carlson, E.H. and Raban, M.,
Chem. Comm. 1971, 656.
24. Isaksson, G. and Sandström, J.,
Acta Chem. Scand. 24, 2565 (1970).
25. Loewenstein, A., Melera, A., Rigny, P. and Walter, W.,
J. Phys. Chem. 68, 1597 (1964).
26. Sandström, J., J. Phys. Chem. 71, 2318 (1967).
27. Shibaeva, R.P. and Atovmyan, L.O.,
Zh. Strukt. Khim. 9, 73 (1968).
28. Lumbroso, H., Pigenet, C., Rossway, H. and Schwenker, G.,
Compt. Rend. Ser. C 266, 1479 (1968).
29. Colleter, J.-C. and Gadret, M., Bull. Soc. Chim. France
1967, 3463; Acta Cryst. B 24, 513 (1968).
30. Lewin, A.H. and Frucht, M., Tetrahedron Lett. 1970, 1079.
31. Staub, H.A. and Lauer, D., Tetrahedron Lett. 1966, 4593.
32. Bedford, G.R., Greatbanks, D. and Rogers, D.B.,
Chem. Comm. 1966, 330.
33. Siddall, III, T. and Garner, R.,
Can. J. Chem. 44, 2387 (1966).
34. Siddall, III, T.H., Pye, E.L. and Stewart, W.E.,
J. Phys. Chem. 74, 594 (1970).
35. Eyman, D.P. and Drago, R.S.,
J. Am. Chem. Soc. 88, 1617 (1966).
36. Badger, R.M. and Bauer, S.H., J. Chem. Phys. 5, 839 (1937).
37. Gramstad, T. and Sandström, J.,
Spectrochim. Acta 25, 31 (1969).
38. Temussi, P.A., Tancredi, T. and Quadrifoglio, F.,
J. Phys. Chem. 73, 4227 (1969).

39. Neuman, Jr., R.C., Woolfenden, W.R. and Jonas, V.,
J. Phys. Chem. 73, 3177 (1969).
40. Blackwood, J.E., Gladys, C.L., Loening, K.L., Petrarca,
A.E. and Rush, J.E., J. Am. Chem. Soc. 90, 509 (1968).
41. Pauling, L., Proc. Nat. Acad. Sci. 14, 359 (1928).
42. Geiger, W., private communication.
43. Gutowsky, H.S., Jonas, J. and Siddall, III, T.H.,
J. Am. Chem. Soc. 89, 4300 (1967).
44. Neuman, R.C. and Jonas, V.,
J. Am. Chem. Soc. 90, 1970 (1968).
45. Pines, A. and Rabinovitz, M., Tetrahedron Lett. 1968, 3529.
46. Jackman, L.M., Kavanagh, T.E. and Haddon, R.C.,
Org. Magn. Resonance 1, 109 (1969).
47. Drakenberg, T. and Forsén, S.,
J. Phys. Chem. 74, 1 (1970).
48. Drakenberg, T., Dahlqvist, K.-I. and Forsén, S.,
Acta Chem. Scand. 24, 694 (1970).
49. Neuman, R.C., Roark, D.N. and Jonas, V.,
J. Am. Chem. Soc. 89, 3412 (1967).
50. Weil, J.A., Blum, A., Heiss, A.H. and Kinnaird, J.K.,
J. Chem. Phys. 46, 3132 (1967).
51. Walter, W., Maerten, G. and Rose, H.,
Ann. Chem. 691, 25 (1966).
52. Carlsson, L.-O., Acta Chem. Scand. 26, 21 (1972).
53. Hobson, R.F., Reeves, L.W. and Shaw, K.N.,
J. Phys. Chem. 77, 1228 (1973).
54. Janssen, M.J., Rec. Trav. Chim. 79, 454 (1960).
55. Janssen, M.J., Rec. Trav. Chim. 79, 1066 (1960).
56. Sandström, J., Svensk. Kem. Tidskrift 72, 612 (1960).
57. Katagiri et al. Quoted in Hosoya, H., Tanaka, J. and
Nagakura, S., Bull. Chem. Soc. Japan 33, 850 (1960).
58. Kasha, M., Disc. Faraday Soc. 9, 14 (1950).
59. Brealey, G.J. and Kasha, M.,
J. Am. Chem. Soc. 77, 4462 (1955).
60. Pimentel, G.C., J. Am. Chem. Soc. 79, 3323 (1957).
61. Sandström, J., Acta Chem. Scand. 16, 1616 (1962).
62. Sandström, J. and Uppström, B.
Acta Chem. Scand. 19, 2432 (1965).

63. Douglas, J.E., Rabinovitch, B.S. and Looney, F.S.,
J. Chem. Phys. 23, 315 (1955).
64. Kende, A.S., Izzo, P.T. and Fulmor, W.,
Tetrahedron Lett. 1966, 3697.
65. Downing, A.P., Ollis, W.D. and Sutherland, I.O., Chem.
Comm. 1967, 143; ibid. 1968, 1053; J. Chem. Soc. (B)
1969, 111.
66. Crabtree, J.H. and Bertelli, D.J.,
J. Am. Chem. Soc. 89, 5384 (1967).
67. Dewar, M.J.S., "The Molecular Orbital Theory of Organic
Chemistry", McGraw-Hill Book Company, Inc., 1969, p. 181.
68. Cavitt, S.B., Sarrafizadeh, H. and Gardner, P.D.,
J. Org. Chem. 27, 1211 (1962).
69. Fries, K. and Brandes, E., Ann. Chem. 542, 48 (1939).
70. Filar, L.J. and Winstein, S., Tetrahedron Lett. 1960, 9.
71. Freudenberg, K., Angew. Chem. 68, 84 (1956).
72. Freudenberg, K., Grion, G. and Harkin, J.M.,
Angew. Chem. 70, 743 (1958).
73. Freudenberg, K. and Werner, H.K.,
Chem. Ber. 97, 579 (1964).
74. Smith, W.B., Watson, W.H. and Chiranjeevi, S.,
J. Am. Chem. Soc. 89, 1438 (1967).
75. Wheland, G.W., "Resonance in Organic Chemistry", John
Wiley and Sons, New York, 1955, p. 98.
76. Wennerbeck, I. and Sandström, J.
Org. Magn. Resonance 4, 783 (1972).
77. Mannschreck, A. and Koelle, V., Tetrahedron Lett. 1967,
863.
78. Kessler, H., Chem. Ber. 103, 973 (1970).
79. Herbig, K., Huisgen, R. and Huber, H.,
Chem. Ber. 99, 2546 (1966).
80. Sieveking, H.U. and Lüttke, W.,
Angew. Chem. 81, 432 (1969).
81. Smyth, C.P., "Dielectric Behavior and Structure",
McGraw-Hill Book Company, Inc., 1955.
82. Pariser, R. and Parr, R.G.,
J. Chem. Phys. 21, 466 (1953).
83. Pariser, R. and Parr, R.G.,
J. Chem. Phys. 21, 767 (1953).

84. Pople, J.A., Trans. Faraday Soc. 49, 1375 (1953).
85. Roothaan, C.C.J., Rev. Mod. Phys. 23, 69 (1951).
86. Parr, R.G., J. Chem. Phys. 20, 239 (1952).
87. Goeppert-Mayer, M. and Sklar, A.L.,
J. Chem. Phys. 6, 645 (1938).
88. Pariser, R., J. Chem. Phys. 21, 568 (1953).
89. Koutecky, J., Paldus, J. and Zahradnik, R.,
J. Chem. Phys. 36, 3129 (1962).
90. Hinze, J. and Jaffé, H.H.,
J. Am. Chem. Soc. 84, 540 (1962).
91. Fabian, J., Theor. Chim. Acta 12, 200 (1968).
92. Fabian, J., Mehlhorn, A. and Tröger, G.,
Theor. Chim. Acta 9, 140 (1967).
93. Nishimoto, K. and Mataga, N.,
Z. Phys. Chem. (Frankfurt) 12, 335 (1957).
94. Mulliken, R.S., J. Phys. Chem. 56, 292 (1952).
95. Rasch, G., Z. Chem. 2, 347 (1962).
96. Mulliken, R.S., Rieke, C.A., Orloff, D. and Orloff, H.,
J. Chem. Phys. 17, 1248 (1949).
97. Fischer-Hjalmars, I. and Sundbom, M.,
Acta Chem. Scand. 22, 607 (1968).
98. Skancke, P.N., Acta Chem. Scand. 18, 1671 (1964).
99. Forsén, S. and Skancke, P.N. in "Selected Topics in
Structure Chemistry", Universitetsforlaget, Oslo, 1967,
p. 229.
100. Dewar, M.J.S., Harget, A.J. and Harget, F.R.S.,
Proc. Roy. Soc. London A 315, 443 (1970).
101. Fischer-Hjalmars, I., Tetrahedron 19, 1805 (1963).
102. Ghirvu, C.I., Gropen, O. and Skancke, P.N.,
Acta Chem. Scand. 25, 2023 (1971).
103. Liljefors, T., Thesis, Lunds Universitet, 1973.
104. Gleicher, G.J. and Arnold, J.C.,
Tetrahedron 29, 513 (1973).
105. Harris, R.K. and Spragg, R.A., Chem. Comm. 1967, 362.
106. Fateley, W.G., Harris, R.K., Miller, F.A. and
Witkorosky, R.E., Spectrochim. Acta 21, 231 (1965).
107. Wennerbeck, I., Acta Chem. Scand. 27, 258 (1973).
108. Cookson, R.C. and Wariyar, N.S., J. Chem. Soc. 1956, 2302.

109. Knapp, G.G. and Orloff, H.D., Fr. Patent, 1,328,010
(Chem. Abstr. 59: P12715d).
110. Grammaticakis, P., Bull. Soc. Chim. France 1964, 924.
111. v. Braun, J., Ber. 37, 2685 (1904).
112. Vogel, A.I., "A Textbook of Practical Organic Chemistry",
2nd ed., Longmans, Green and Co., 1951, p. 864.
113. v. Auwers, K. and Niemeyer, F., J. prakt. Chem. 110,
160 (1925).
114. Papini, P., Auzzi, G. and Bambagiotti, M.,
Gazz. Chim. Ital. 1968, 245.
115. Hantzsch, A., Chem. Ber. 24, 502 (1891).
116. Katritzky, A.R., Øksne, S. and Boulton, A.J.,
Tetrahedron 18, 777 (1962).
117. Holmberg, B. in "Svedberg Memorial Volume", Uppsala,
1944, p. 299.
118. Jepson, J.B., Lawson, P. and Lawton, V.D.,
J. Chem. Soc. 1955, 1791.
119. Jensen, K.A. and Crossland, I.,
Acta Chem. Scand. 17, 144 (1963).
120. Åkerblom, E., Acta Chem. Scand. 21, 846 (1967).
121. Edwards, H.D. and Kendall, J.D., Brit. Patent 624,028
(Chem. Abstr. 44: P5605d).

